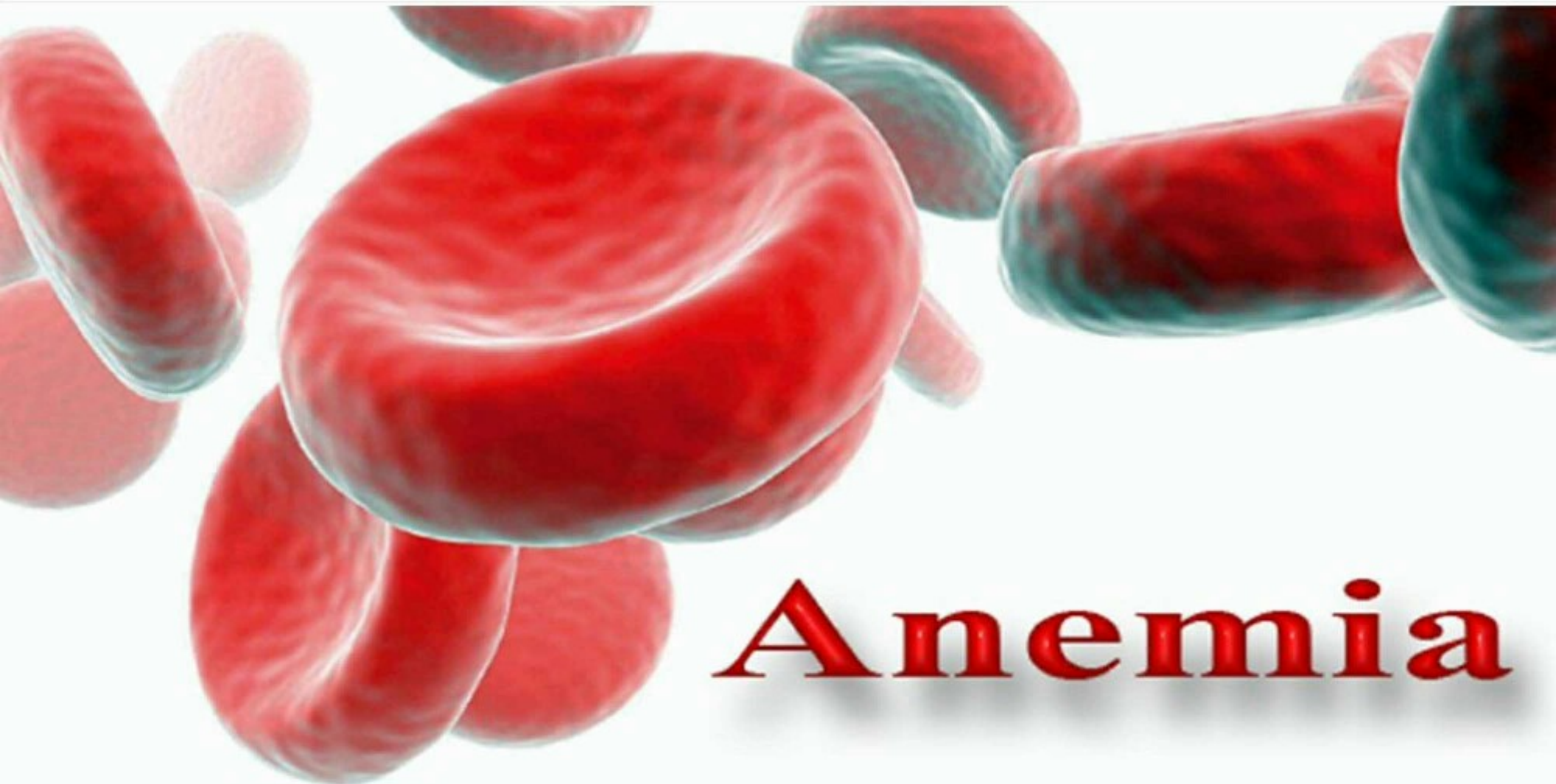


General Manifestations of Anemia



Anemia

Dr. Tarek Abdelhamid M.D.

VISIT...

LANZAROTE
Caliente.COM

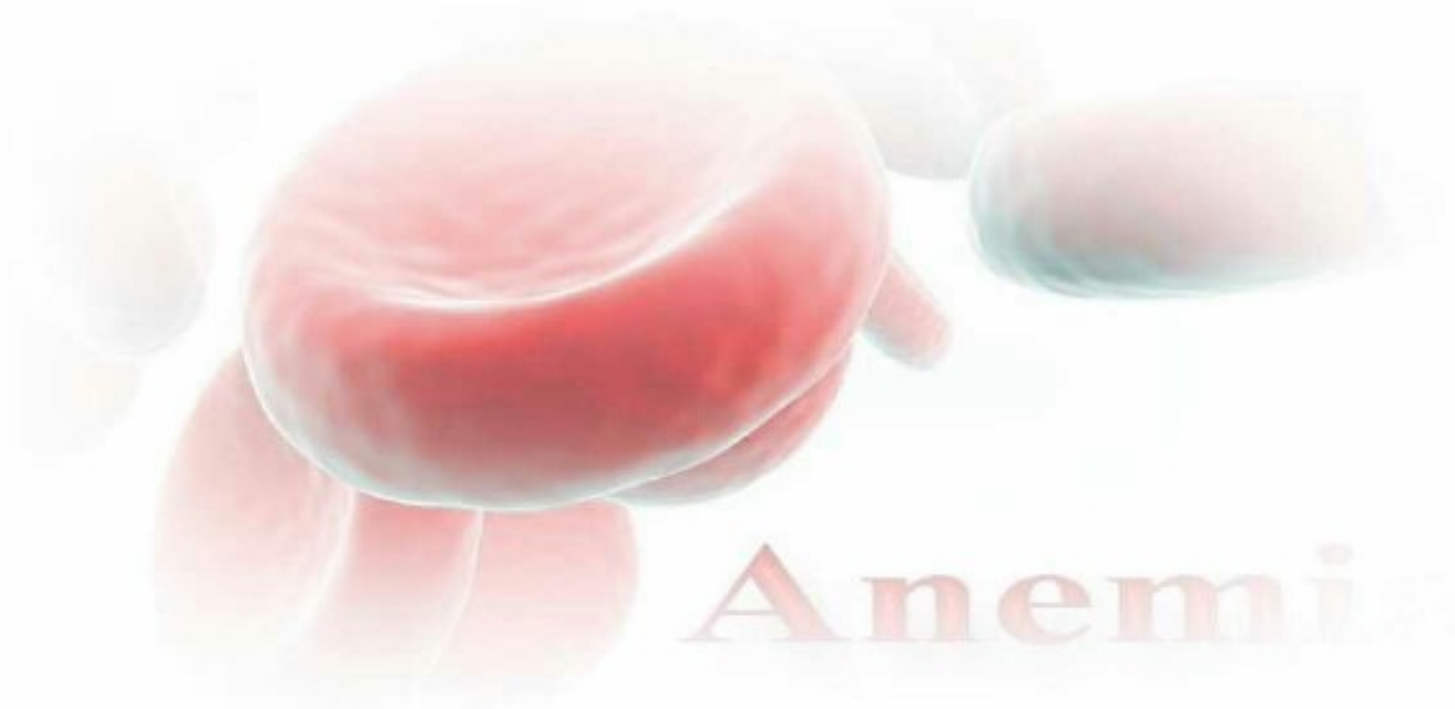
تحذير هام

هذا الفيديو و جميع الرسوم التوضيحية المتاحة فى هذا الموقع هم تحت حماية قانون الملكية الفكرية

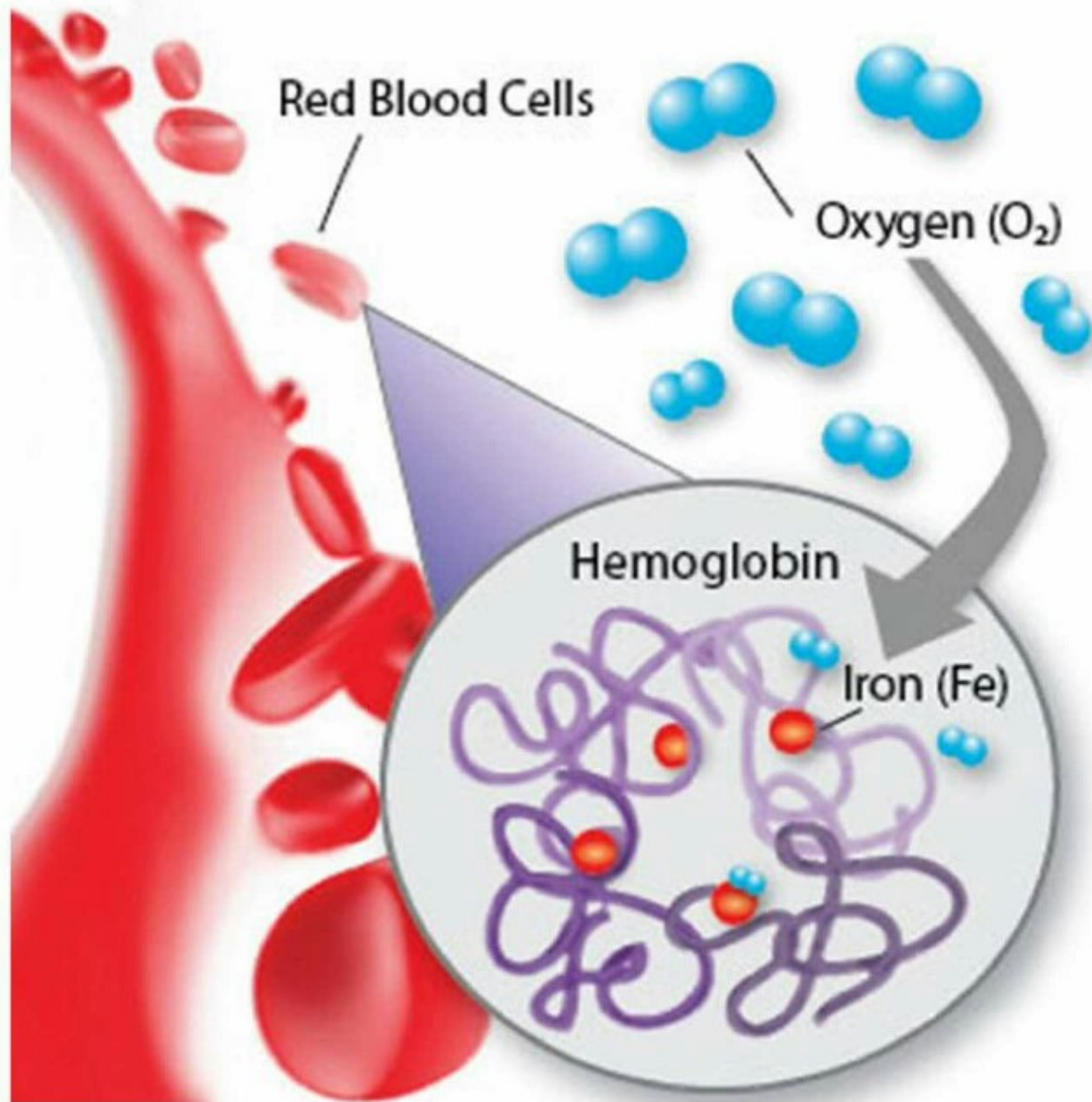
هذا الفيديو و جميع الرسوم التوضيحية المتاحة فى هذا الموقع هم تحت حماية قانون الملكية الفكرية و لا يحق لأحد إستخدامه او تحميله أو إستنساخه أو إعادة طبعه أو طبع أجزاء منه بدون إذن مسبق من الدكتور طارق عبد الحميد (أو من ينوب عنه قانونياً) . و من يتعدى على الملكية الفكرية المذكورة فسوف يتعرض للمسائلة القضائية عن جريمة إنتهاك حقوق الملكية الفكرية. و إستخدام الفيديوهات و المادة العلمية المذكورة مكفول فقط لمستخدم واحد فقط و لأخذ تصريح إستخدام لأكثر من شخص برجاء الإتصال بالدكتور طارق عبد الحميد

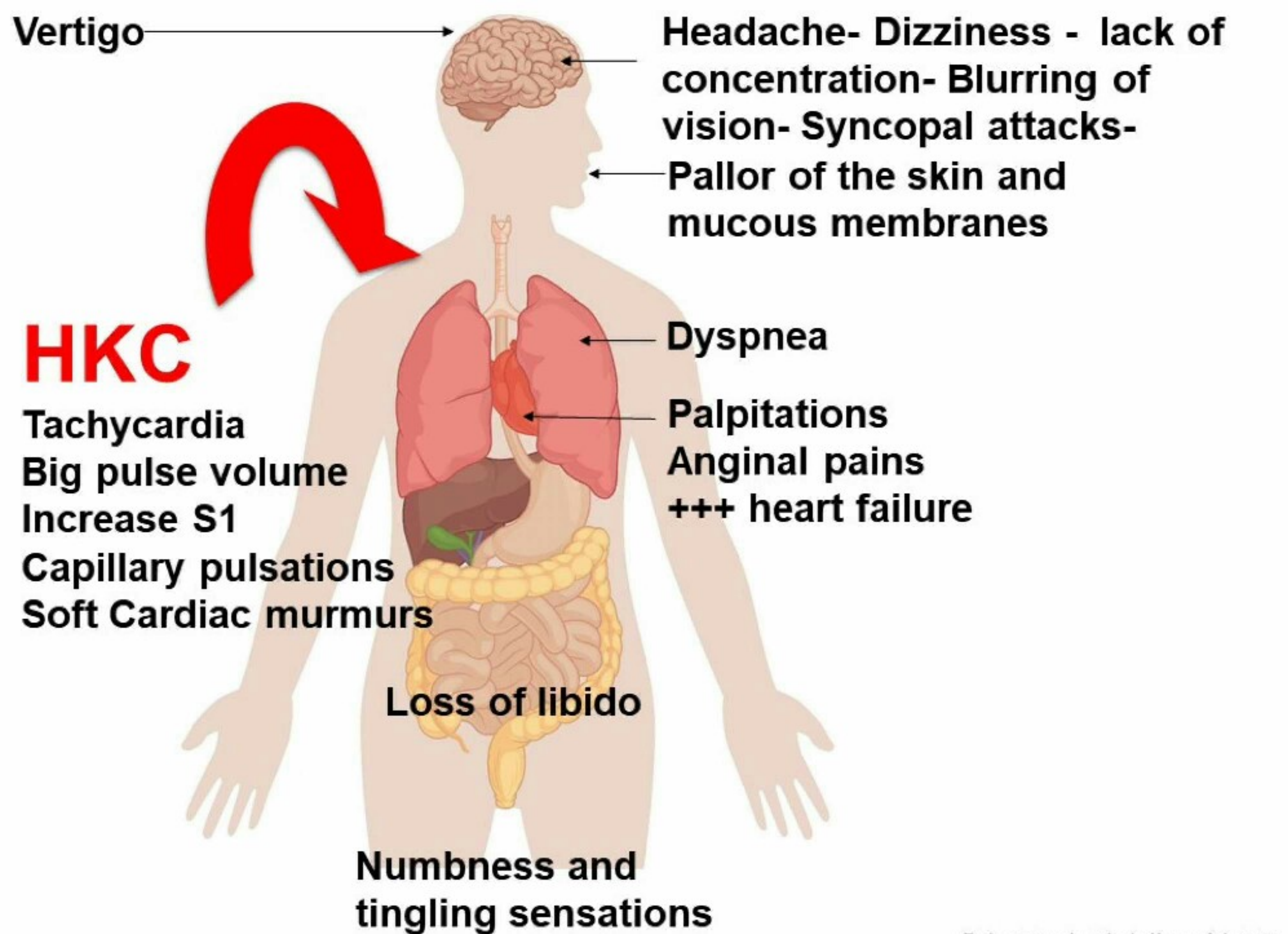
Definition

Anemia is defined as
Hemoglobin
less than 13.5 g/dl in males
OR/ less than 12 g/dl in
females



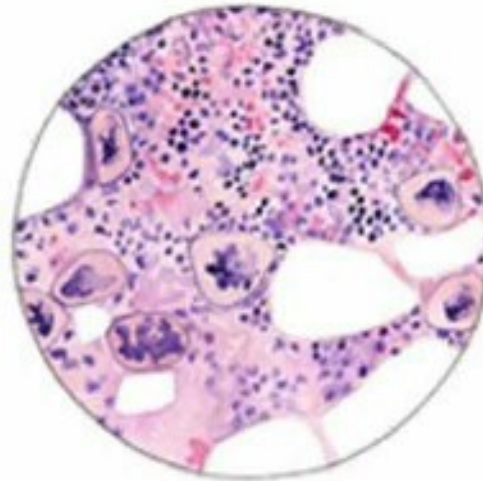
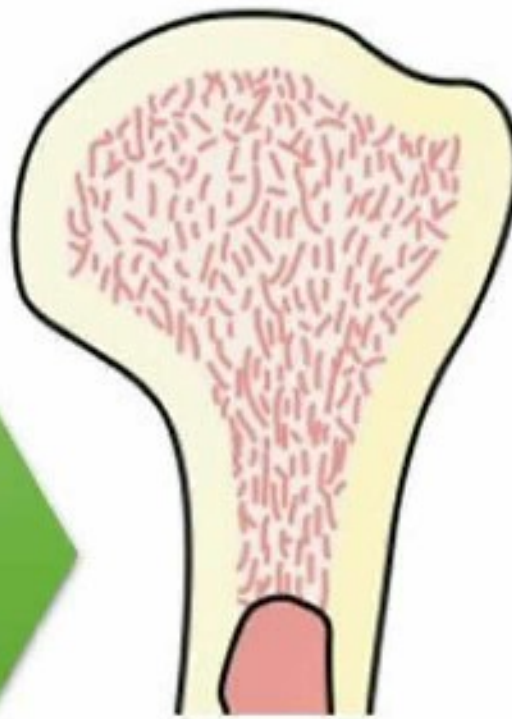
Effects





Causes

Nutrition



Production



Cells

Causes

Nutritional factors



Iron deficiency
B12 deficiency
Folate deficiency

**Inability of the
Bone Marrow to
produce cells**



Aplastic anemia
Renal Failure
**Bone Marrow
infiltration**



**Destruction
of red cells**



Hemolysis

Investigations

CBC

Hemoglobin %

MCV

MCHB

MCHB%

Reticulocyte count

Vitamin levels

Investigations to detect the cause



Treatment

Treatment of the cause



Iron Deficiency Anemia



Definition

A form of anemia caused by iron deficiency



Aetiology



Intake

Children and malnutrition



Absorption

① Pernicious anemia causing Achlorhydria

② Duodenal bypass

③ Increased Phytate or Tannic Acid in diet



Needs

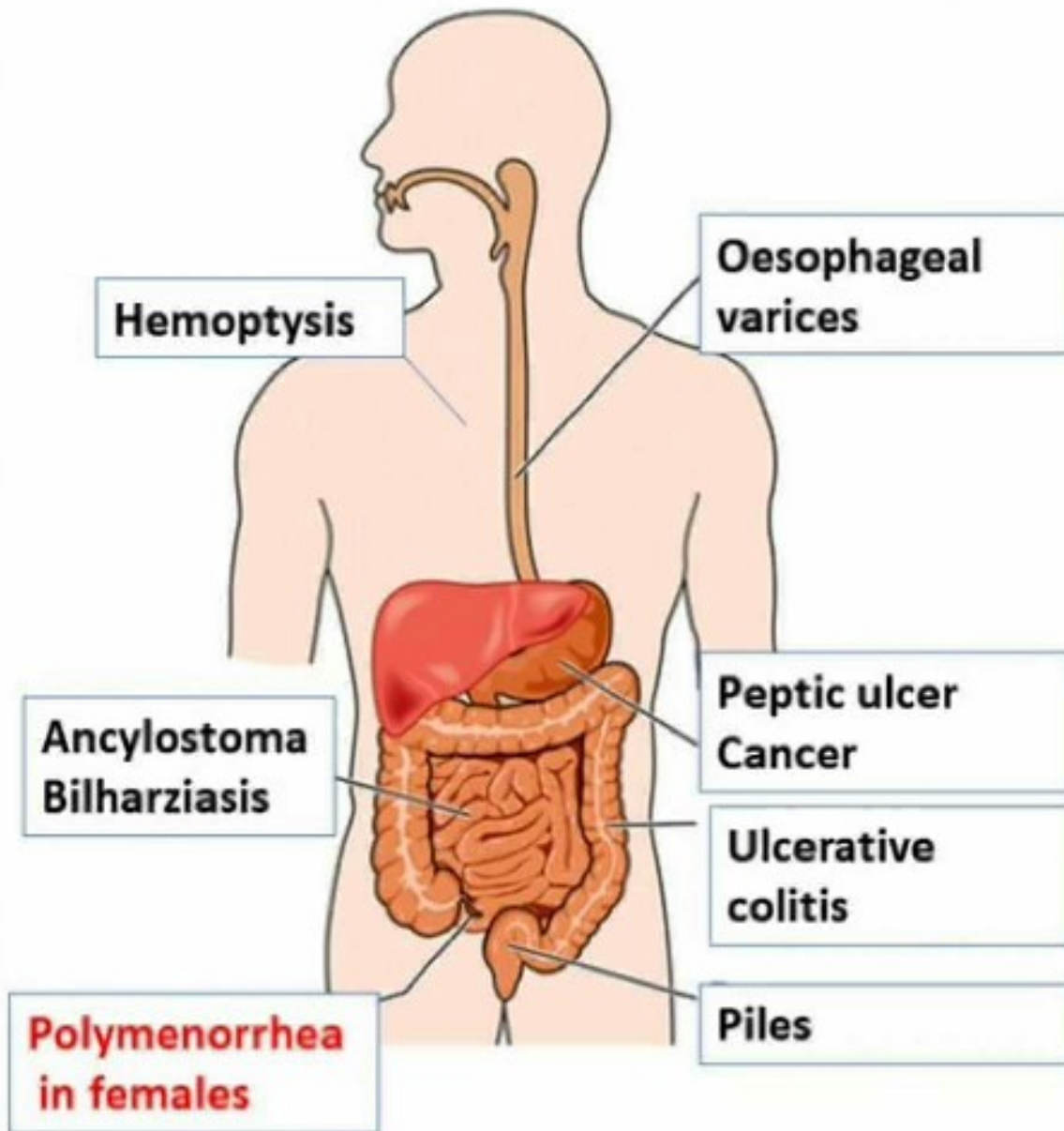
Pregnant women
Puberty



Blood loss



Aetiology Causes of Chronic blood loss



Clinical Picture

① General manifestations of anemia: Weakness- Headache- Palpitation,.....,.....

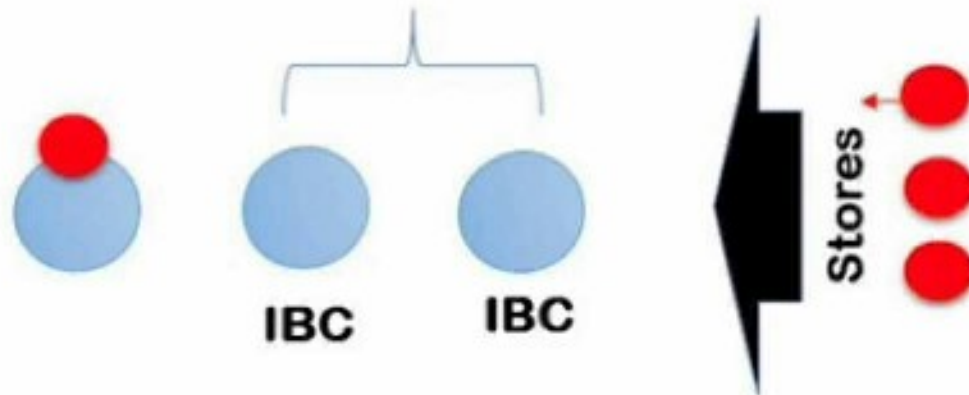
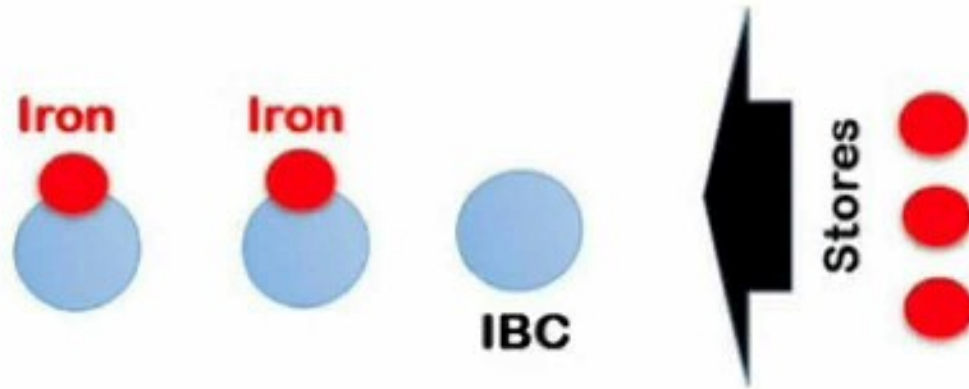
② Glossitis-Stomatitis-Gastritis



③ Koilonychia



Mechanism



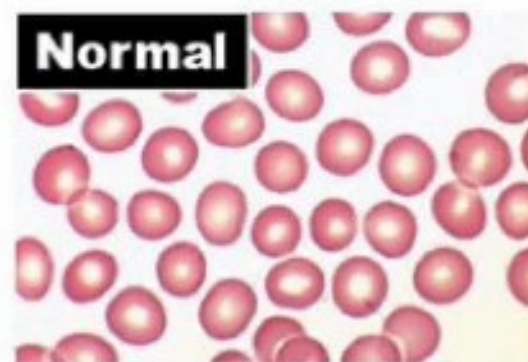
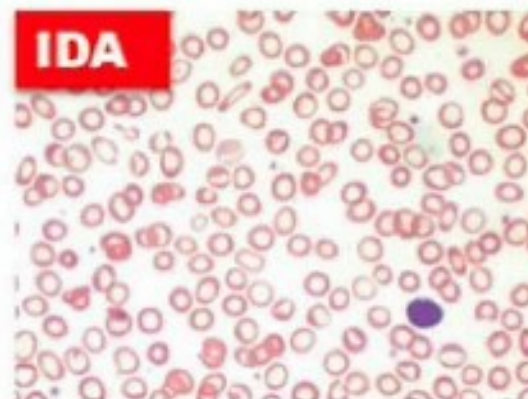
Special Investigations

**Microcytic
Hypochromic
Anemia**

↓ **Iron Level**
↑ **IBC**
↓ **Iron Stores**

↑ **FEP**

**Reticulocytosis
after iron therapy**



Treatment

Iron Replacement Therapy

① Oral therapy is the rule

Fe SO₄ 200 mg TDS or Fe Gluconate 600 mg TDS

Give it during meals to avoid gastric irritation

Add vitamin C to enhance iron absorption

Continue the therapy for 6 months to replenish the iron stores as well.

② Parenteral therapy

Indications:

Defective absorption

If you needed rapid correction (e.g. Pregnancy)

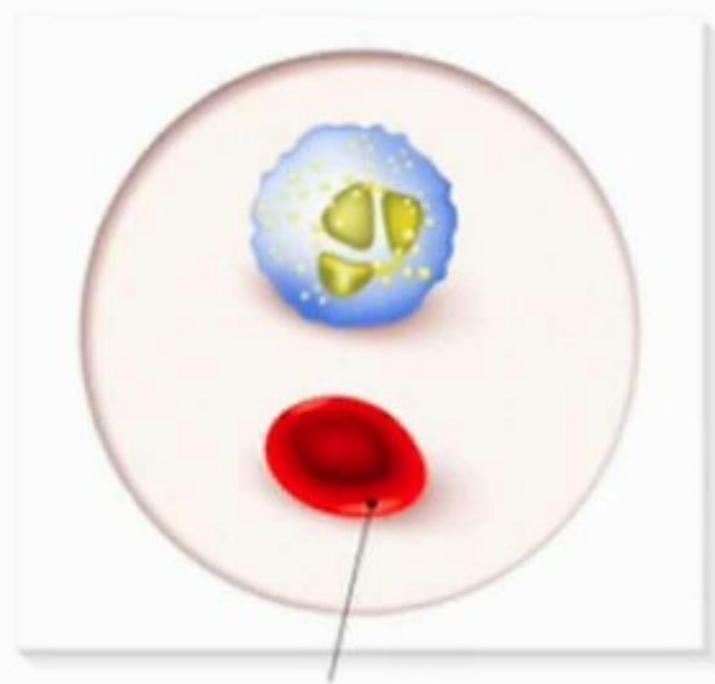
If the patient can not tolerate oral iron

Inflammatory Bowel Disease (IBD)

③ Treatment of the cause (Essential)

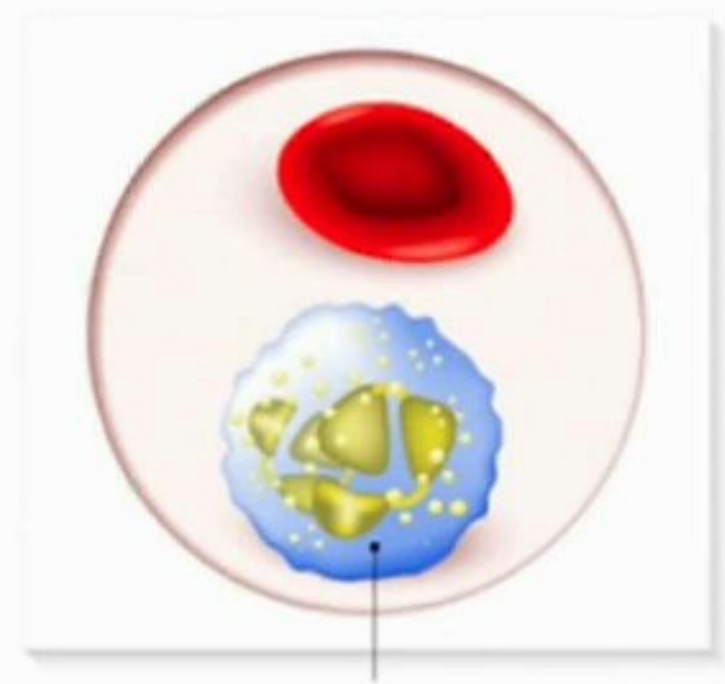
Megaloblastic Anemia

Normal



Red blood cell

Megaloblastic anemia

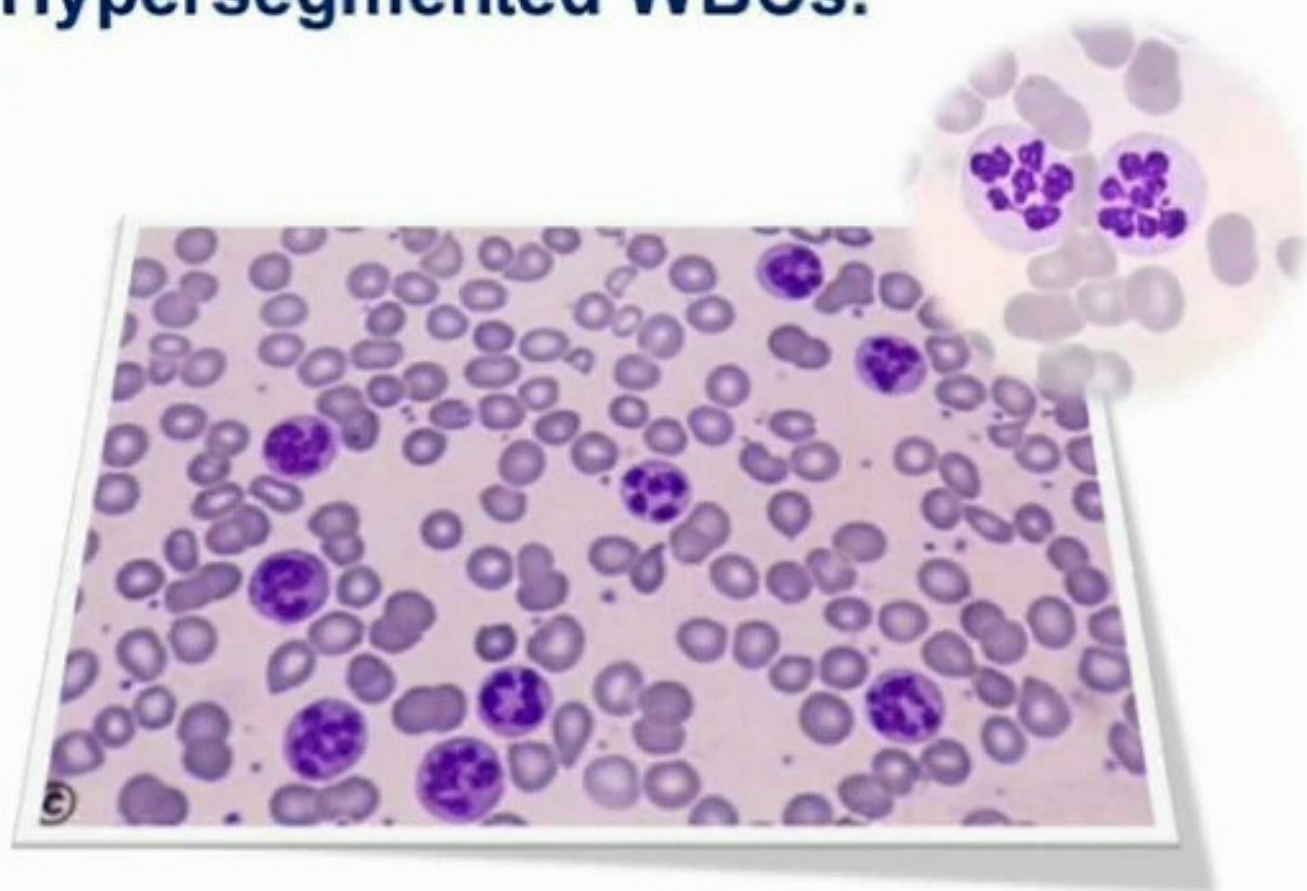


Hypersegmented neutrophils

Definition

A form of anemia characterized by Megaloblastoid and Morphological changes of the blood cells & Bone Marrow.

The condition is typically associated with Hypersegmented WBCs.



Aetiology

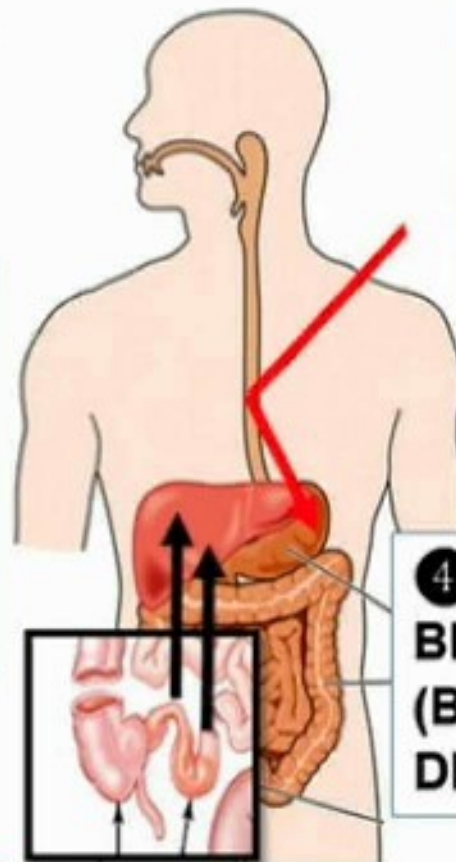


Vitamin B12

① Diminished intake (rare)

⑤ Increased Utilization
Pregnancy
T3++++
MPD
Chronic hemolysis

③ Terminal Ileum Disease
T.B.- Crohn's disease



② Decreased Intrinsic Factor
Autoimmune (Pernicious anemia)
Atrophic gastritis
Gastrectomy

④ Increased Consumption
Blind Loop Syndrome (Bacteria)
DBL (Parasite)

Aetiology

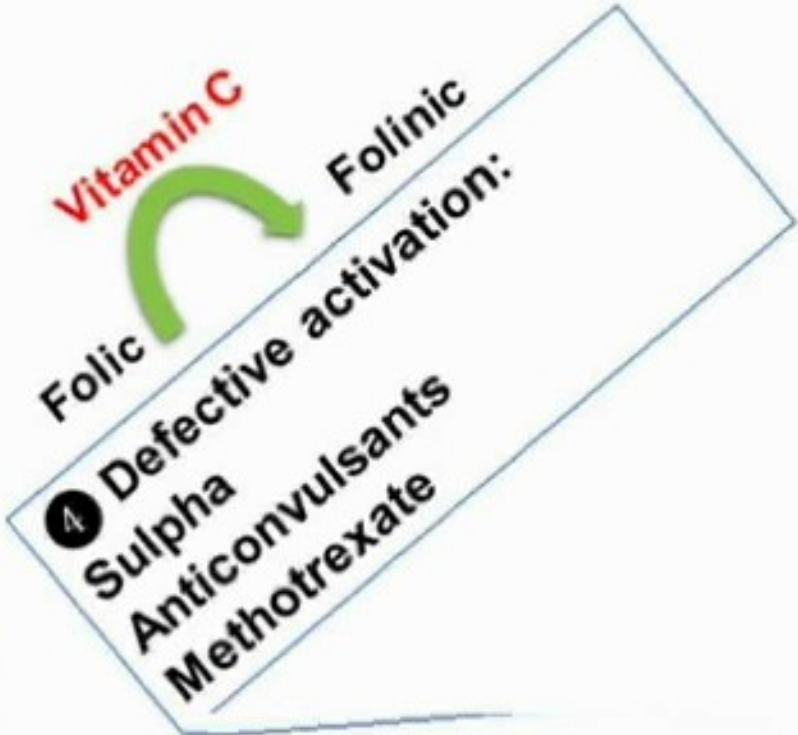
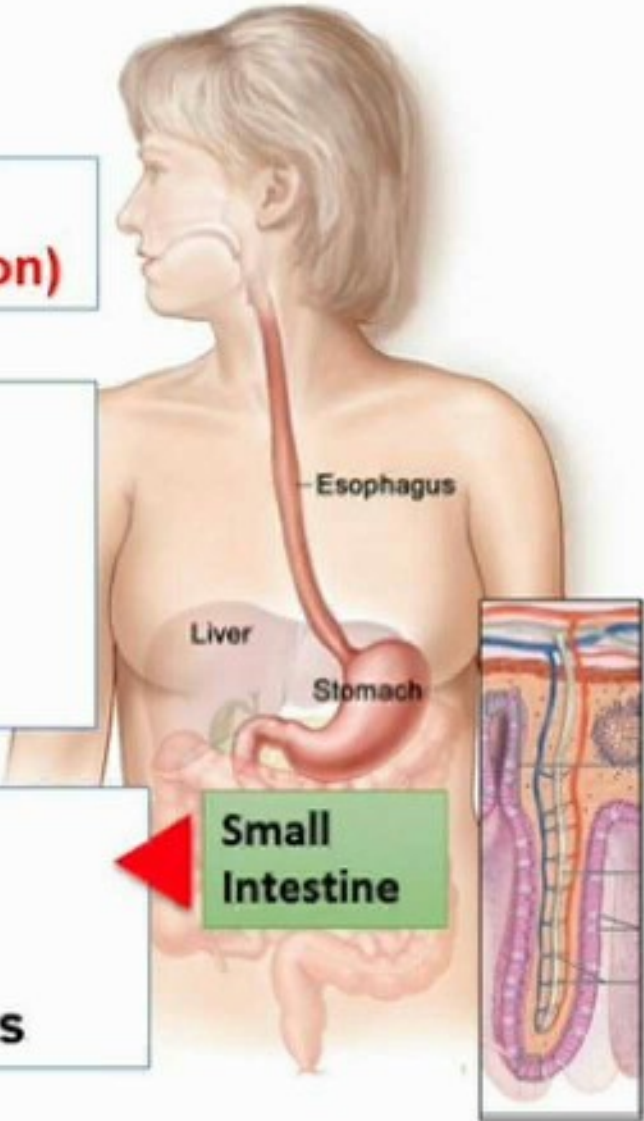


Folic acid

1 Diminished intake (Common)

**2 Increase needs e.g.
Pregnancy
Malignancy
Children**

**3 Diminished absorption
MAS OR
Anticonvulsants**



Mechanism

Homocysteine

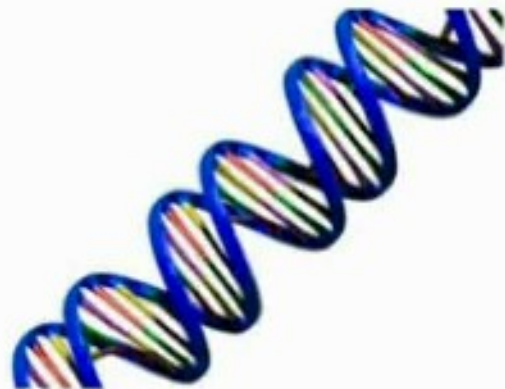


◀ **Vitamin B12** ▶

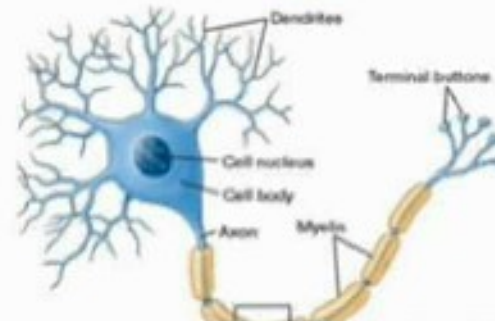


Methylmalonyl CoA

Methionine



Succinyl CoA.



Clinical Picture

① Decreased All blood elements



RBCs: Anemia

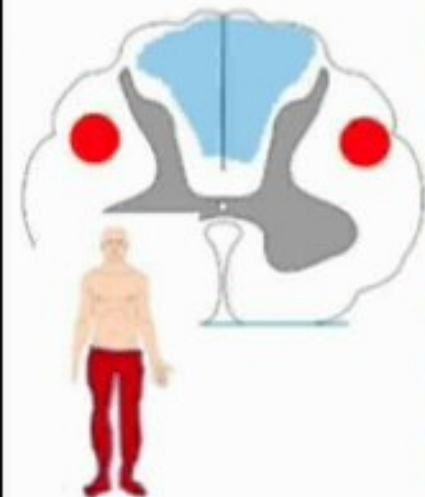


WBCs: Infections



Platelets: Bleeding tendency

② Neurological Manifestations (in Vitamin B12 deficiency)



Pyramidal tract:

Paraparesis

Posterior column:

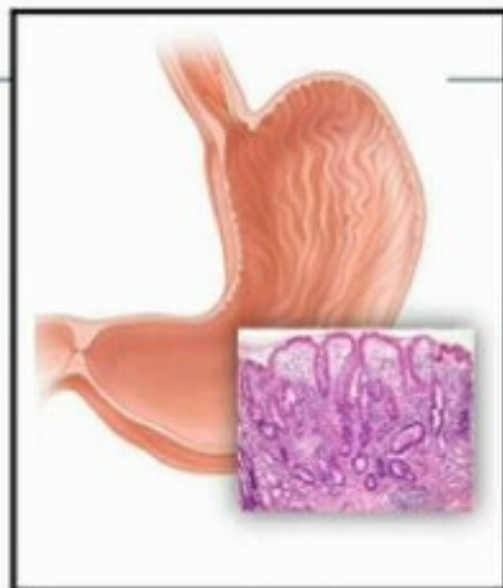
loss of vibration sense

Peripheral nerve:

Paresthesia

Pernicious anemia

- 1 Caused by Anti-IF & Anti Parietal Cell Abs
.....► **Achlorhydria**
- 2 Usually More than 40 Ys...► Increased Cardiac Manifestations
- 3 Atrophic gastritis may...► Cancer Stomach (Monitor occult blood in stools)
- 4 Autoimmune...►?! Hepatomegaly and associated autoimmune diseases
- 5 If NO response to Vitamin B12 therapy..► think of concomitant IDA due to cancer stomach or co-associated Hypothyroidism (Hashimoto Thyroiditis)



Special Investigations

**Macrocytic
Hyperchromic
Anemia**



MCV



MCHb



MCHC%

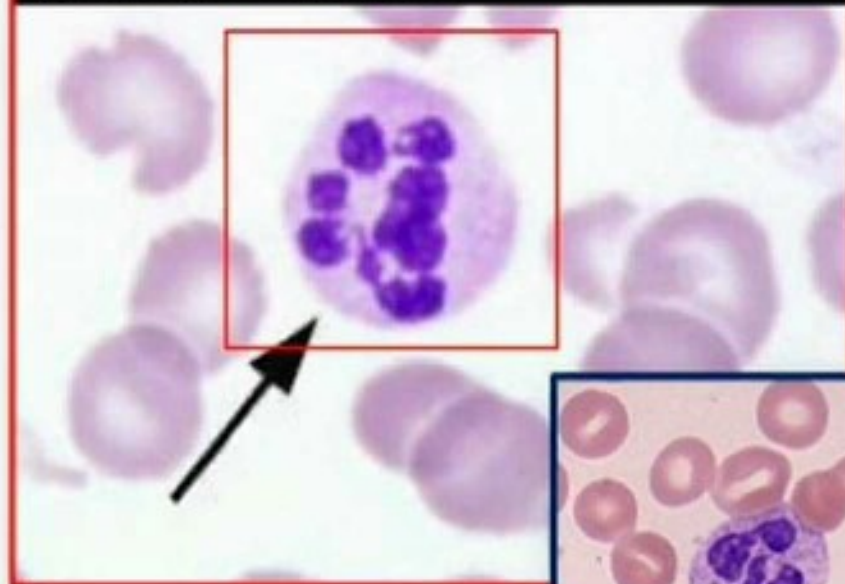
**Low Red Cell
B12 or Folic acid**

**Hypersegmented
WBCs**



**LDH &
Indirect
Bilirubin**

Hypersegmented WBCs



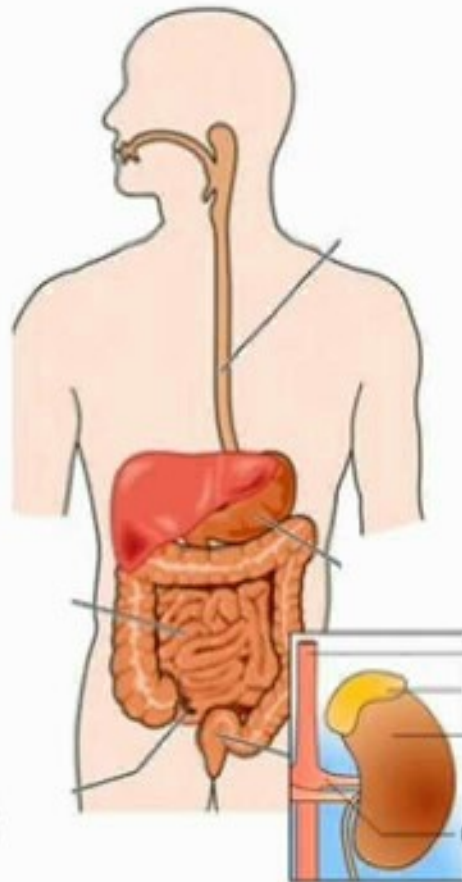
Normal

Shilling test for B12 deficiency

1 2 μg oral
Radioactive B12

2 1000 μg
Vitamin B12 IM
to fill the stores

3 Normally
5-40% RA B12 is
absorbed and
excreted in urine



4 If less than 5% are
excreted in urine you
must consider IF
deficiency or disease
of the terminal ileum

5 Give IF orally....If the
problem is corrected
then the cause is
deficiency of the IF

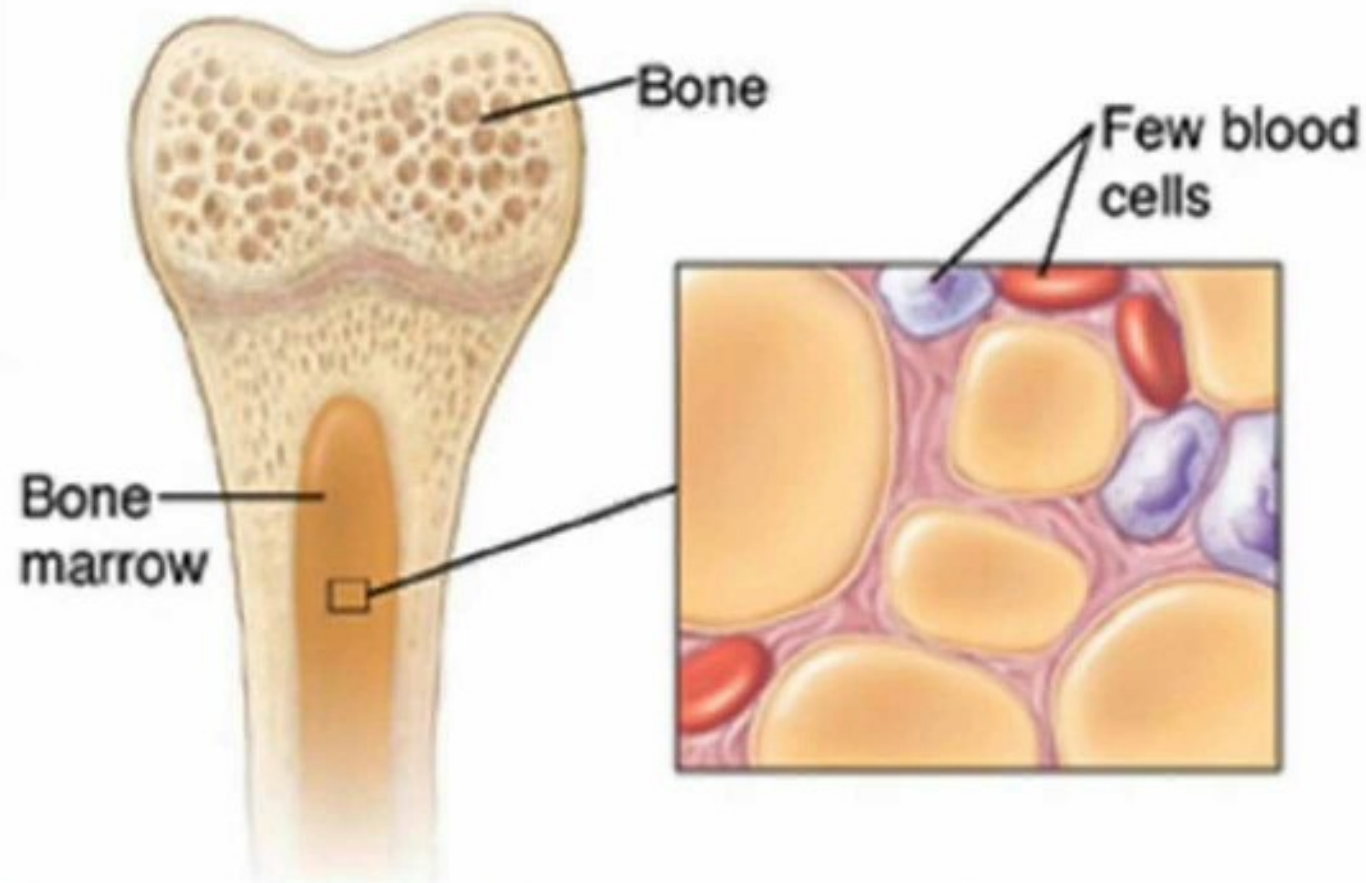
Treatment

Replacement Therapy

- ① 1000 μg Vitamin B12/12 hours then per week then monthly
PLUS Folic acid 5 mg day
- ② **NEVER** give folic acid alone in B12 deficiency as it can +++++ the neurological Complications
- ③ Treatment of the cause (Essential)

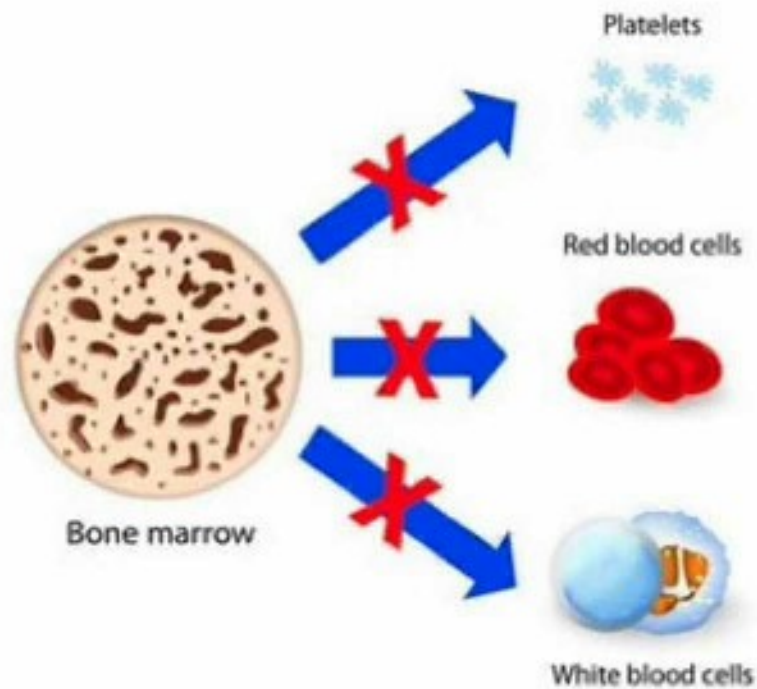


Aplastic Anemia



Definition

A condition characterized by failure of the Bone Marrow pluripotent stem cells to produce blood elements such as RBCs-WBCs- and Platelets.



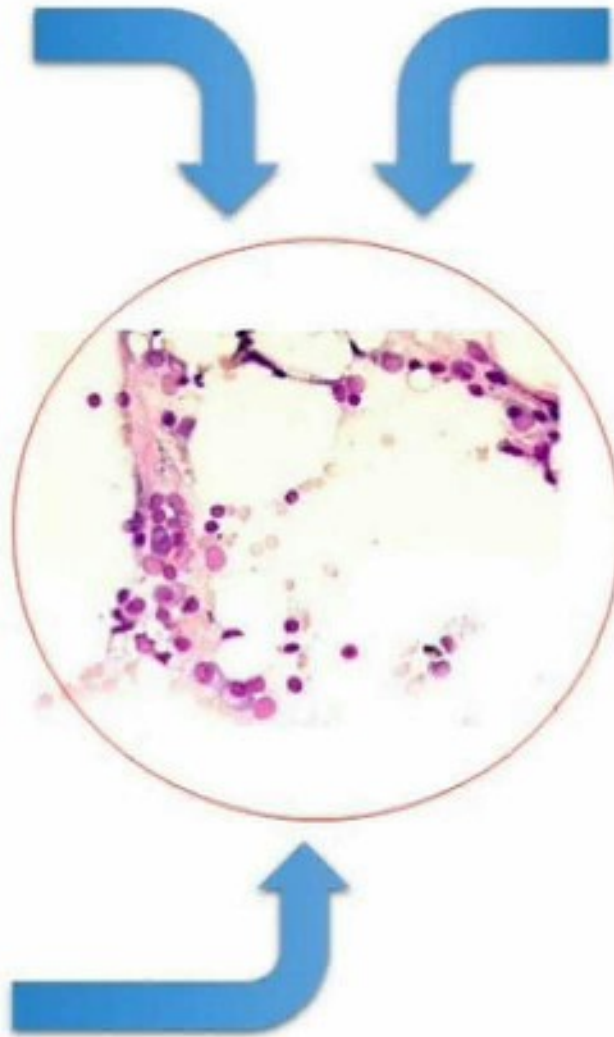
Aetiology

Autoimmune suppression of hematopoiesis by T-Cell mediated mechanisms (Males- 30Ys)

Drugs

Chloramphenicol
Sulpha
Indomethacin
Gold
Tolbutamide
PTU

Irradiation
Chemotherapy
[Cytotoxic Drugs]
Toxins: Benzene-
Insecticides



Clinical Picture

Decreased All blood elements



RBCs: Anemia



WBCs: Infections

**Persistent Sore
Throat With
Necrotic Ulcers
(NO Pus)**



Platelets:
Bleeding tendency



Special Investigations

PCP

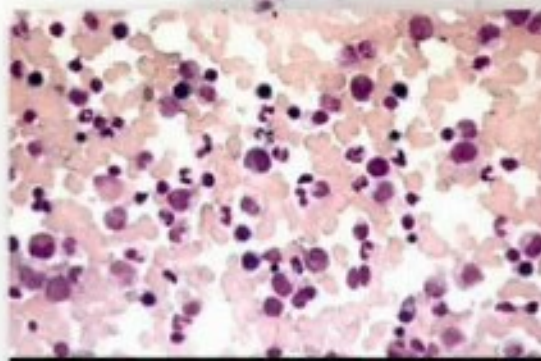
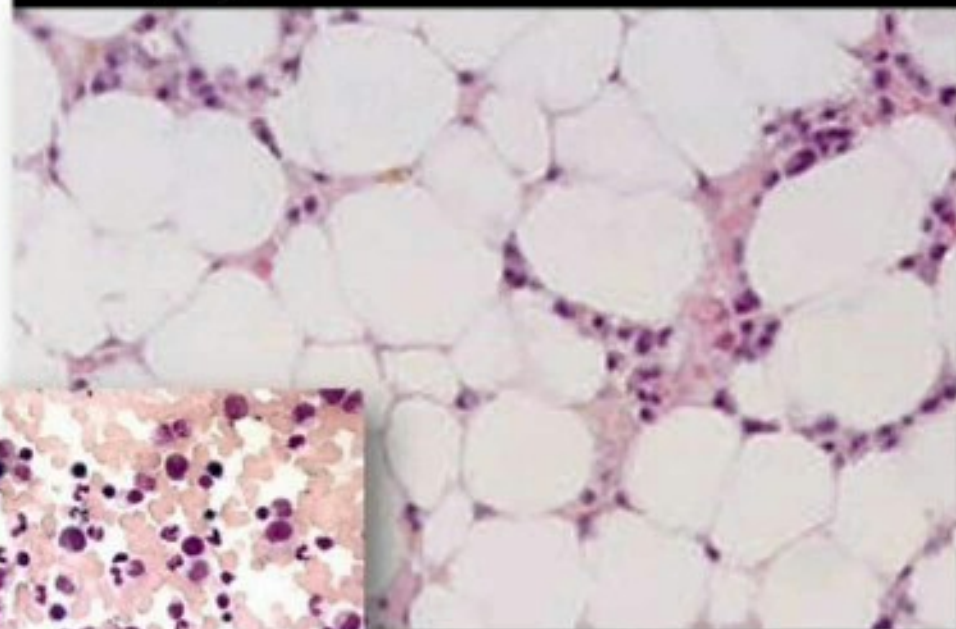
= MCV

Low
Reticulocyte
Count

Empty
Bone
Marrow

Note: Serum iron may be elevated due to
lack of utilization

Empty bone marrow



Normal

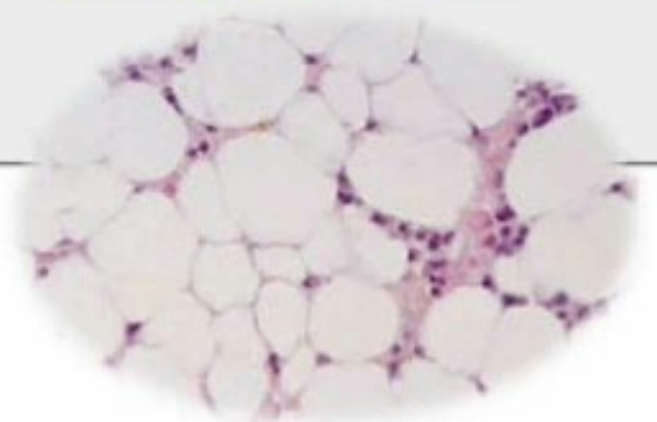
Treatment

Therapeutic Options

- ① **Bone Marrow transplantation** (for Young adults less than 50 Ys who have HLA-matched siblings)
- ② **ATG** + Cyclosporine + Corticosteroids (the latter is to AVOID Serum Sickness secondary to Anti-thymocyte globulin)
- ③ High dose **Cyclophosphamide** in Refractory cases.
- ④ Androgens (to +++++ BM)
- ⑤ **STOP** the offending drug (or chemical) Immediately

Important Note:

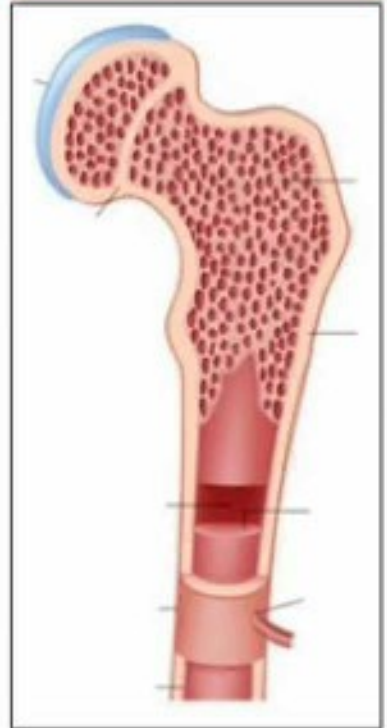
NEVER give Live vaccines to patients with bone Marrow failure.



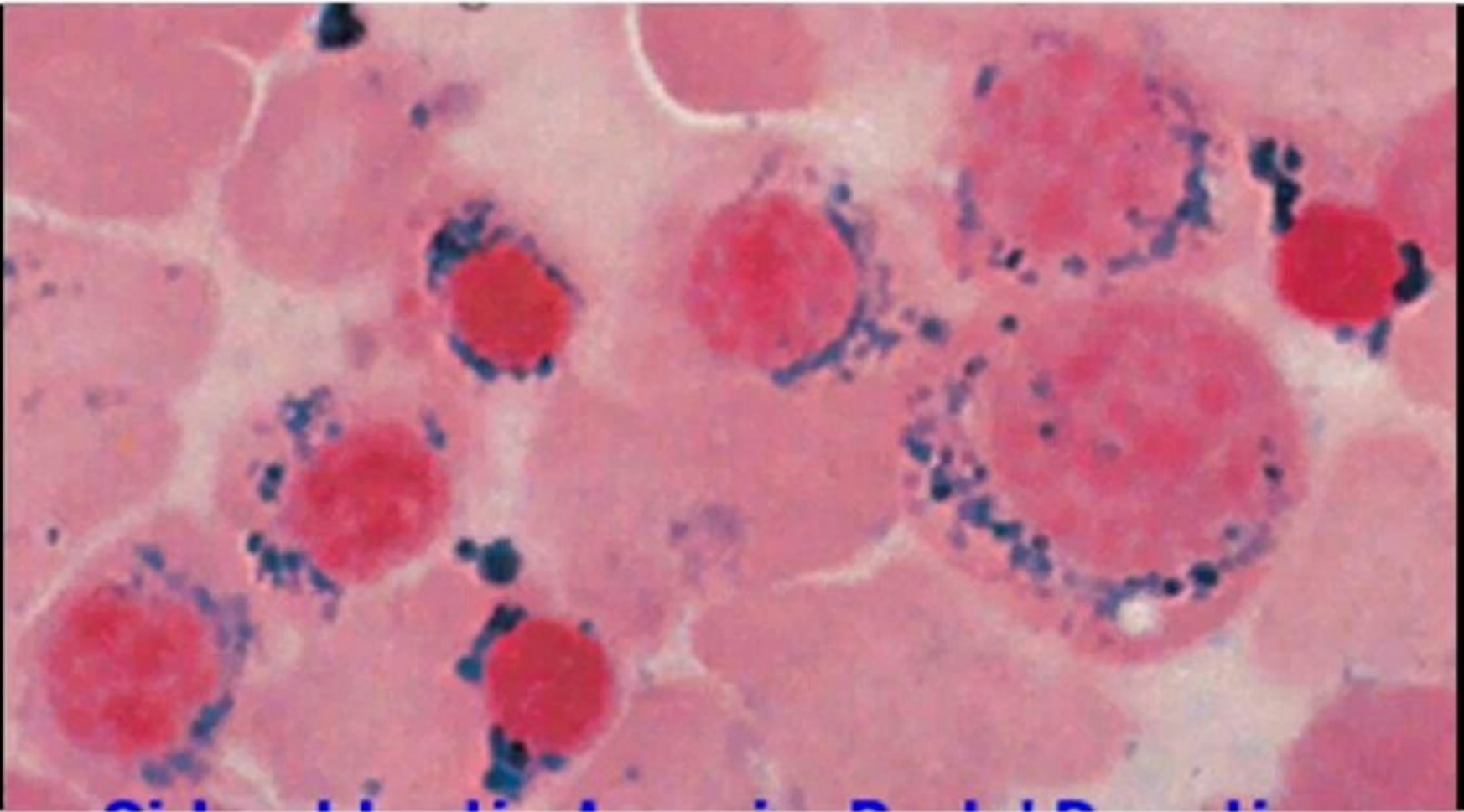
DD of Pancytopenia

- 1 B12 and Folate Deficiency**
- 2 Bone marrow Infiltration**
- 3 Bone Marrow Failure**
- 4 SLE**
- 5 PNH**
- 6 Hypersplenism**

PCP



Sideroblastic Anemia



Definition

A form of anemia caused by inability to incorporate iron into hemoglobin molecule.

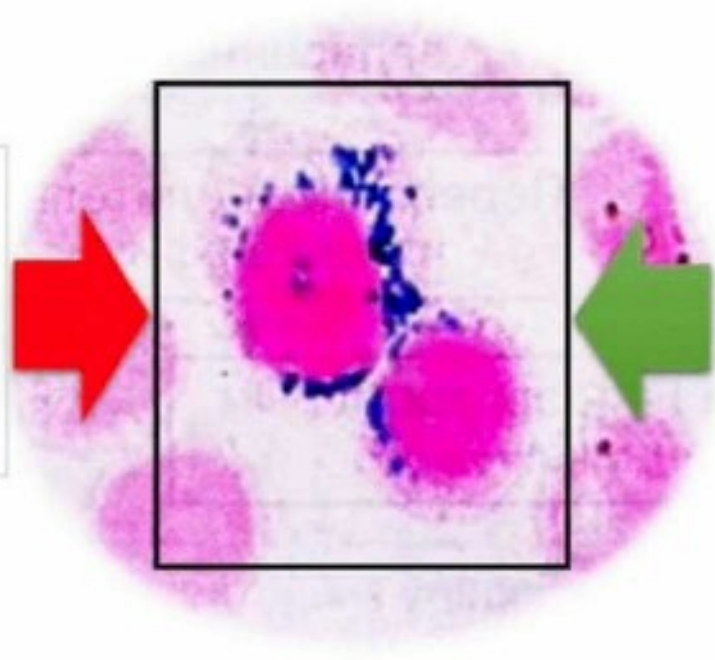
Aetiology

- 1 Hereditary (Males)
- 2 INH
- 3 Chronic lead poisoning
- 4 Rheumatoid arthritis
- 5 **Vitamin B6**
- 6 Alcoholism



Mechanism

**Microcytic
Hypochromic
anemia**

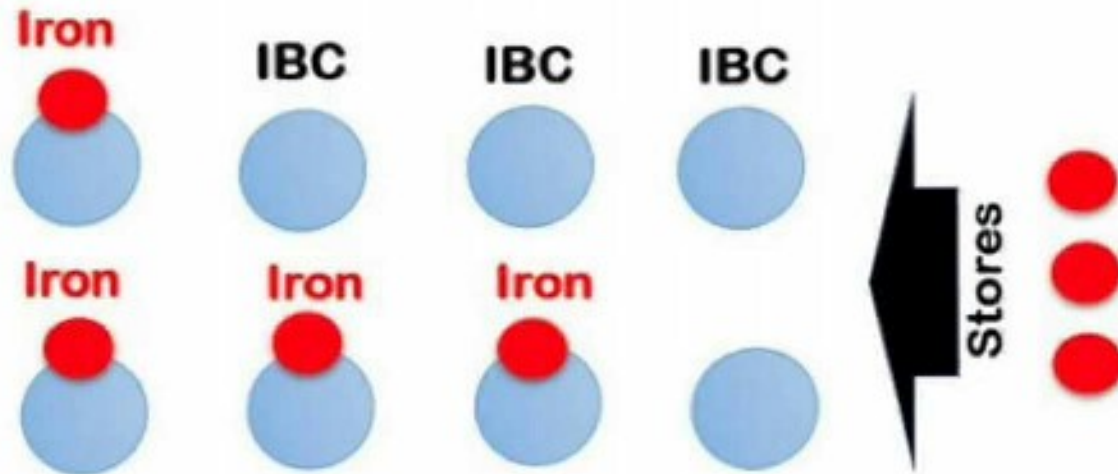


**Ring
sideroblasts**

Clinical Picture

Anemia associated with the underlying cause.

Laboratory results in Sideroblastic Anemia



Special Investigations



Serum Iron

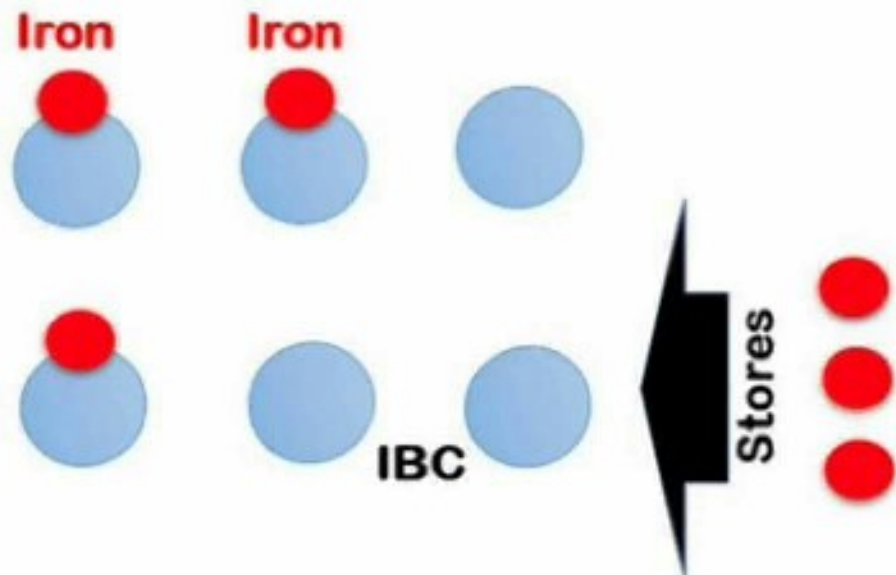


IBC



Iron Stores

**Dimorphic
Blood
Picture**



Treatment

Treatment of the cause is essential.

High dose **Vitamin B6** may improve some hereditary cases.

Pyridoxine 100 mg TDS

Hemolytic Anemia (General)



Definition

A group of disorders characterized by diminished life span of RBCs (Normally 120 days).

Aetiology

Intra-corpuscular



Extra-corpuscular

Drugs

Immune

Environmental

Aetiology

Intra-corporcular

① Defects in Hemoglobin

Thalassemia- SCA

② Defects in Enzymes

G6PD Deficiency

③ Defects in Shape

Hereditary Spherocytosis

④ Other causes:

PNH- Vitamin B12 Deficiency
(Ineffective Erythropoiesis)

Aetiology

Extra-corporeal

Drugs

Analgesics: Aspirin
(rare)

Antibiotics: Sulpha

Antimalarial:

Primaquine

Anti hypertensives:

Aldomet

Aetiology

Extra-corpuscular

Immune

Drug induced:

Penicillin: haptenic

Stibophen: IBS

Aldomet: autoimmune

Autoimmune:

AIHA

Alloimmune:

Rh Incompatibility

Incompatible Blood

Transfusion

Aetiology

Extra-corporeal

Environmental

① Mechanical Factors

Hypersplenism

Malignant Hypertension

Artificial Valve

DIC

② +++ Heat (Burns)

③ Irradiation

④ Infections

Malaria

IMN

Septicemia

Manifestations of Hemolysis (General)

Anemia



**Pallor-Weakness-
Fatigue-
LCO Symptoms-
(Qualitative)**

Manifestations of Hemolysis (General)

Jaundice

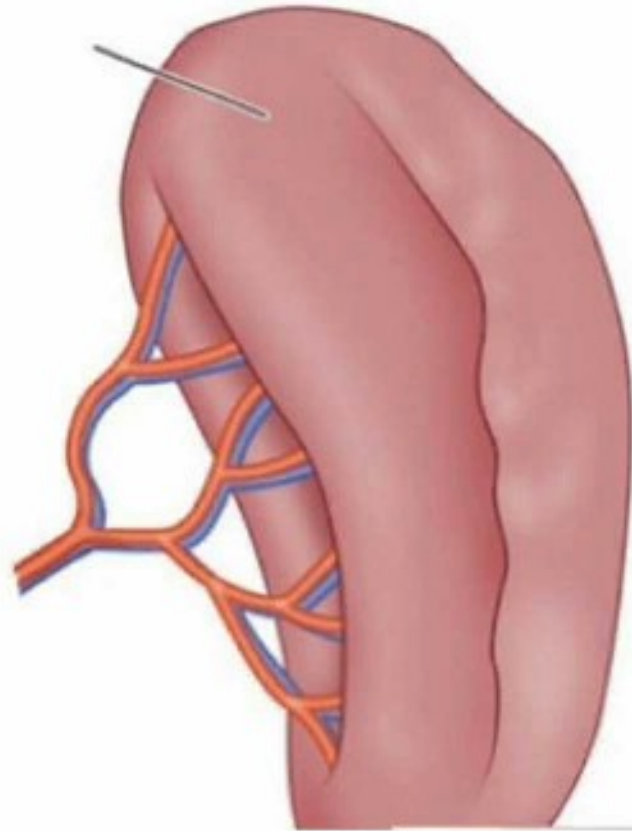


 **Indirect Bilirubin**
Urobilinogen
Stercobilinogen

Manifestations of Hemolysis (General)

+++++

Spleen



Except in
Sickle Cell Anemia

Manifestations of Hemolysis (General)



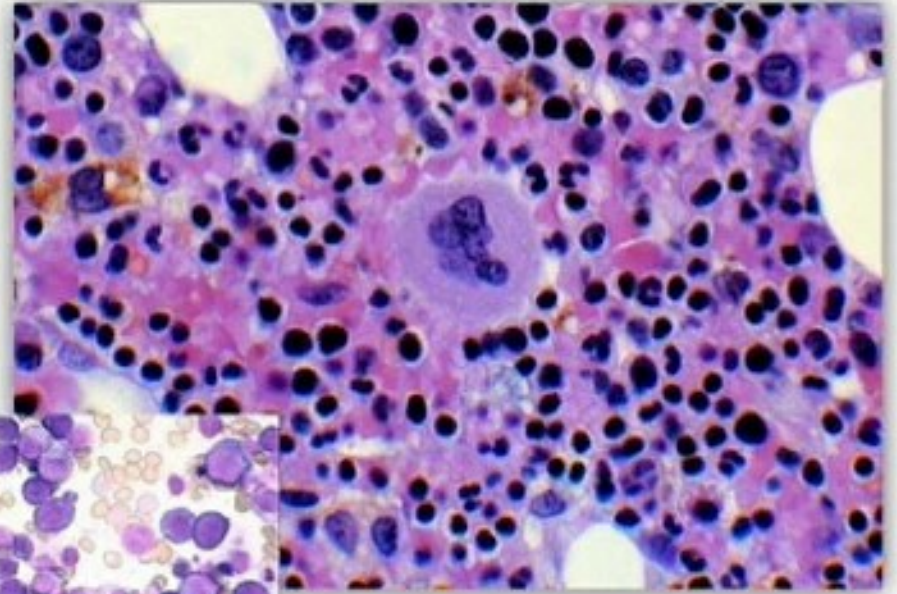
Reticulocytes



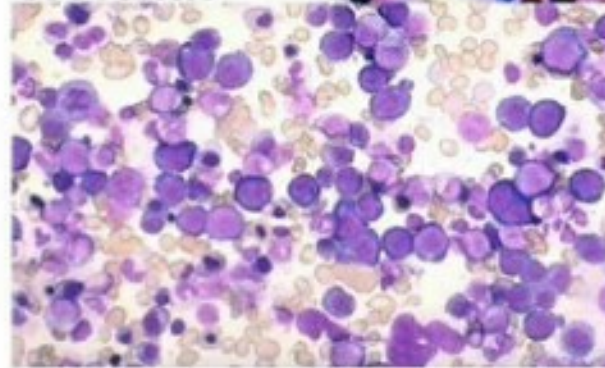
Manifestations of Hemolysis (General)

Hyperplastic Bone Marrow

Hyperplastic Bone Marrow



Normal



Manifestations of Hemolysis (General)

Hemolytic Crisis



- 1 Increase in All manifestations
- 2 Fever
- 3 Rigors
- 4 Abdominal pain
- 5 Dark Urine
- 6 ?! ARF

Note

Aplastic or Hypoplastic crisis may occur if the BM failed suddenly.

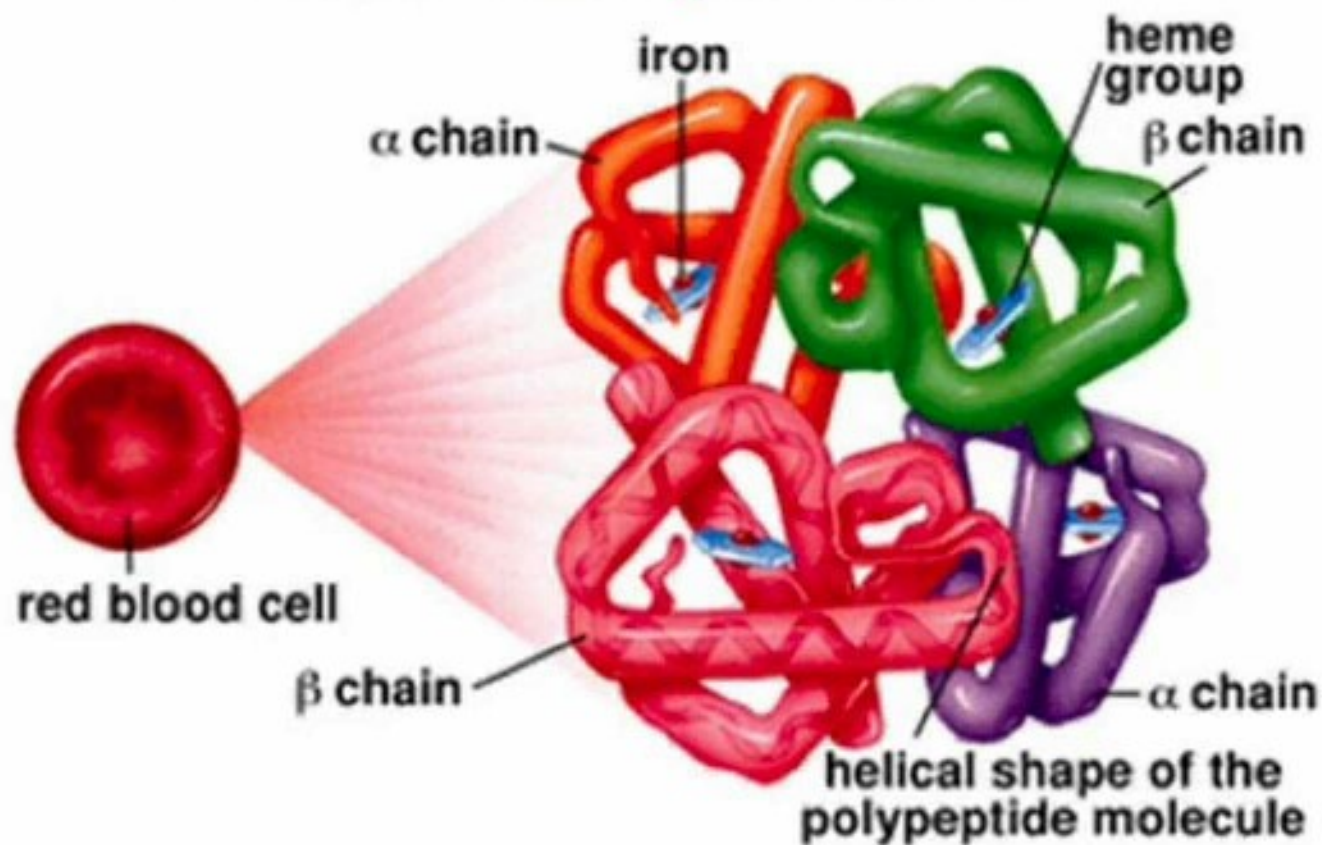
Manifestations of Hemolysis (General)



Hemopexin
Haptoglobin



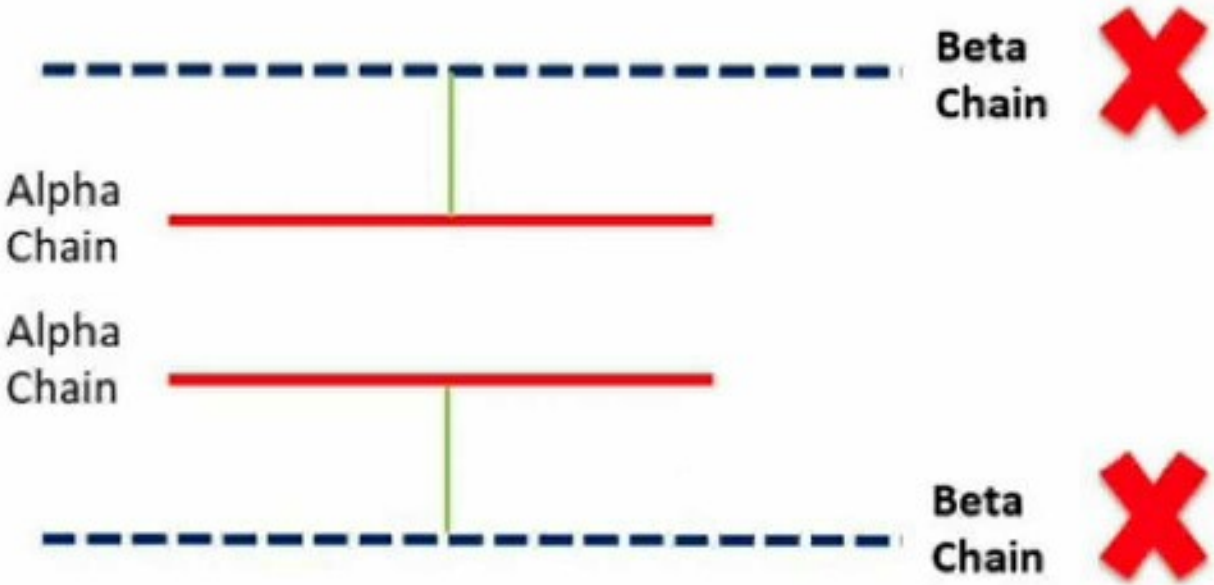
Hemolytic Anemia (Thalassemia)



Definition

A form of hemolytic anemia caused by a defect in the biosynthesis of beta Chains of Hemoglobin molecule.

Aetiology

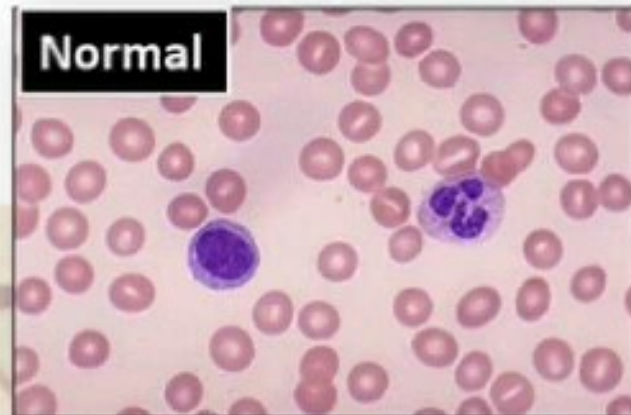
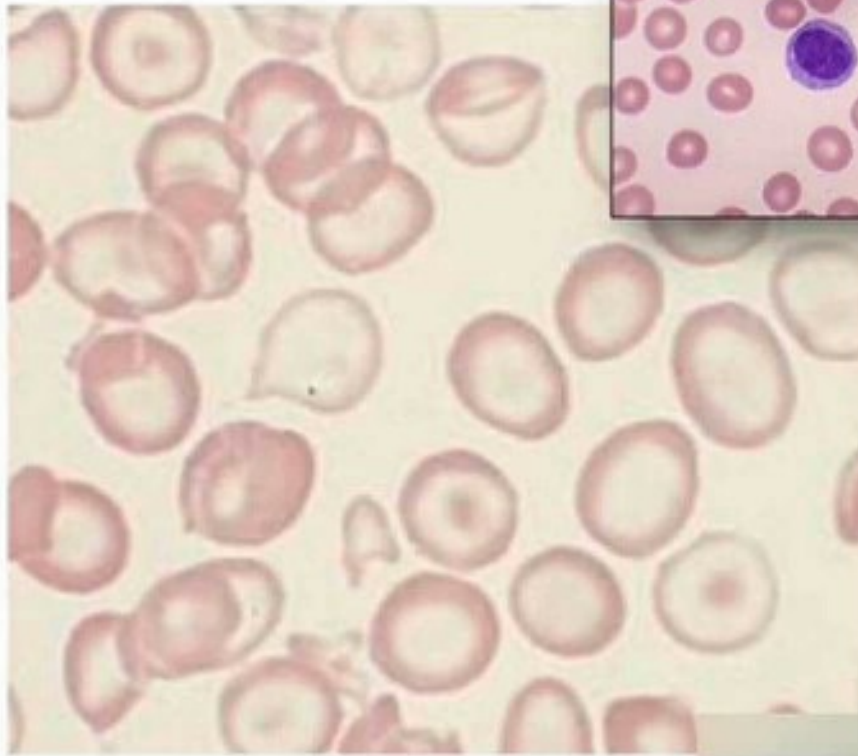


Mechanism

**Defective
hemoglobin
biosynthesis**



**Microcytic
Hypochromic
anemia**

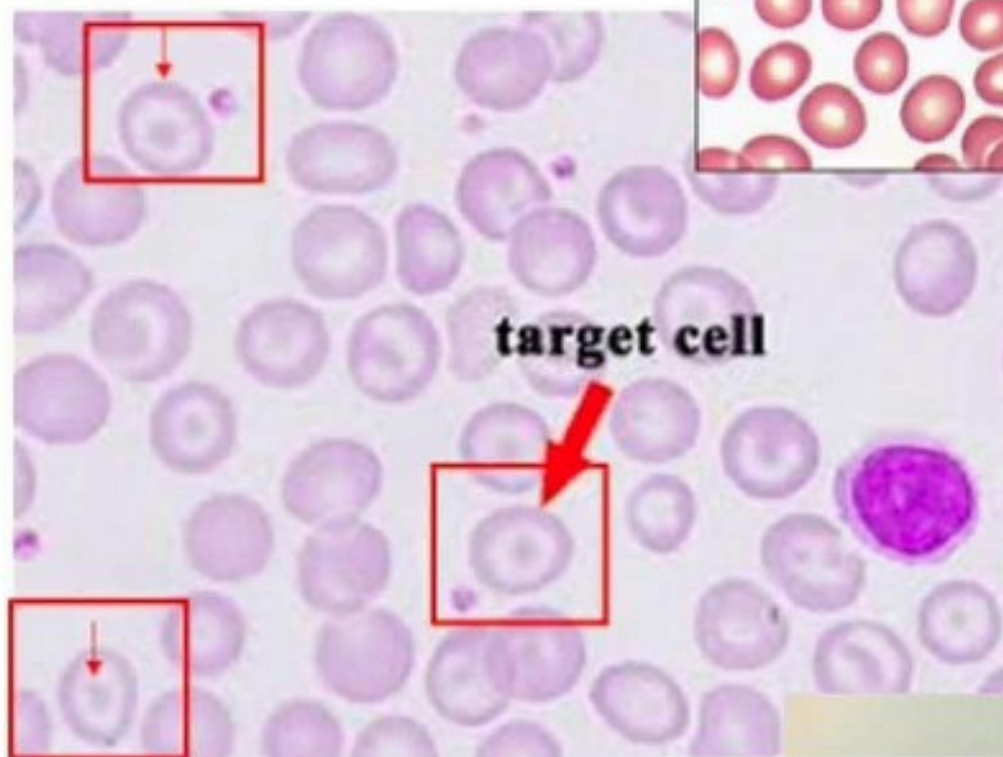


Mechanism

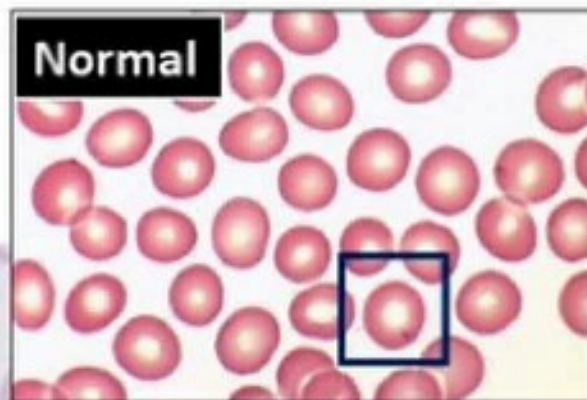
Small amount of
abnormal
hemoglobin in
the cells



Target Cells



Normal

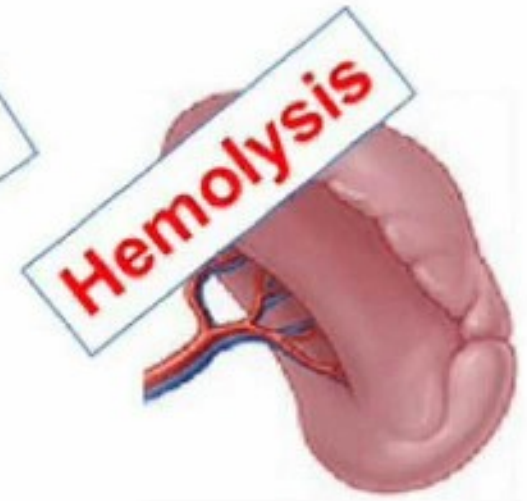
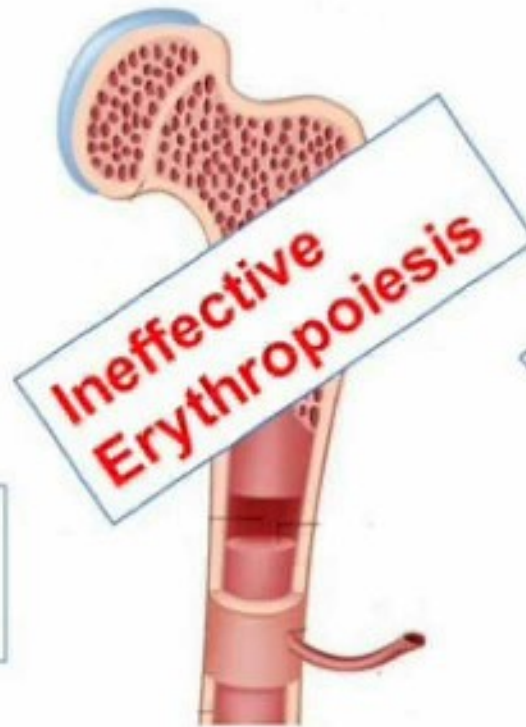


Mechanism

Free alpha chains
Causing RBCs to
be rigid



Destruction of Red
cells both



In the BM
(**Ineffective
Erythropoiesis**)

In the
spleen
(**Hemolysis**)

Mechanism

++++++ Anemia
causes severe
tissue hypoxia



REF



Bone
Marrow
Hyperplasia



Skeletal
Deformities
in children



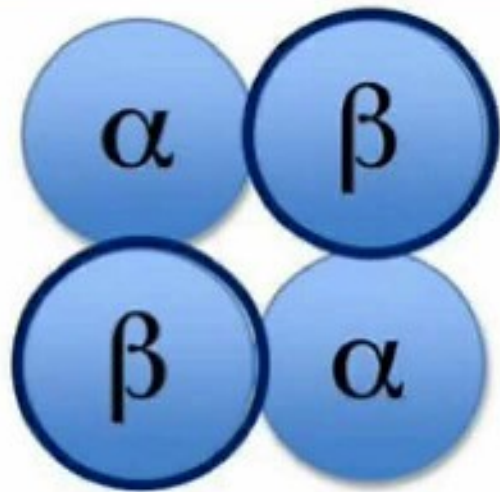
Mongoloid face



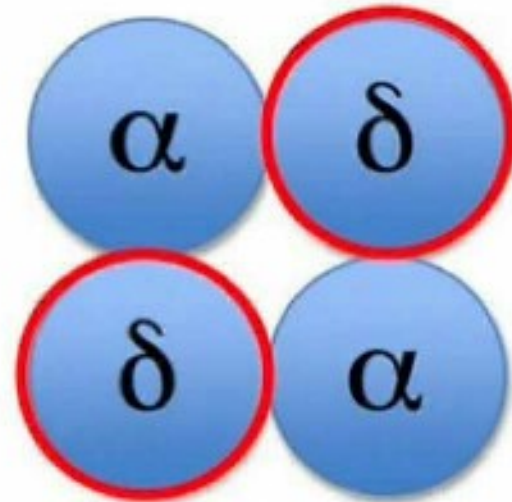
Hair on End Appearance

Mechanism

Inability to produce
normal Adult Hemoglobin
(Alpha + Beta chains)



Hemoglobin F
(Alpha + Gamma Chains)



Clinical Picture

General Manifestations of hemolysis



Pallor

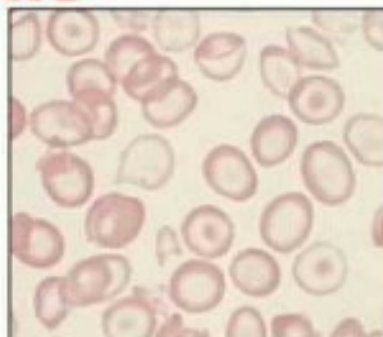
Weakness

+++ Spleen

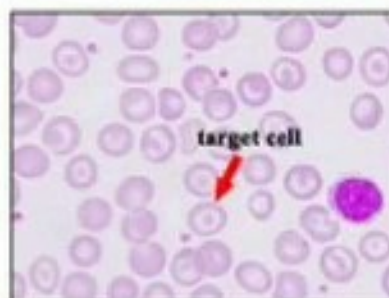
Note: Mongoloid Face (if +++++)

Special Investigations

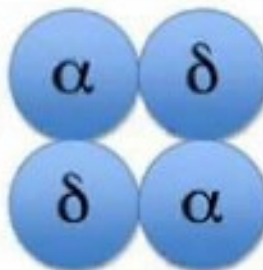
**Microcytic
Hypochromic
Anemia**



Target Cells



Hemoglobin F



**Skull X Ray:
Hair on End
Appearance**

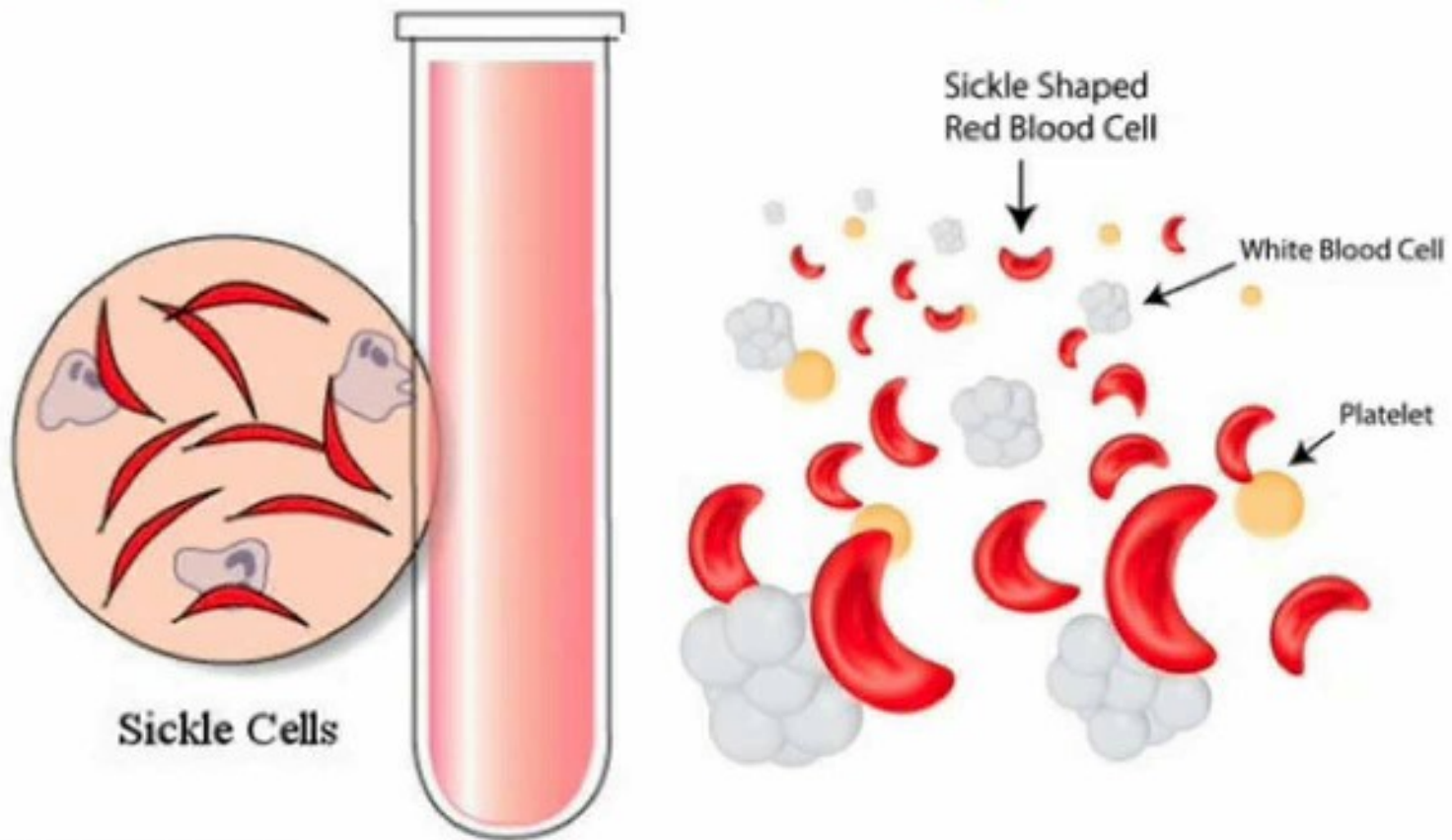


Treatment

Therapeutic Options for Thalassemia Major

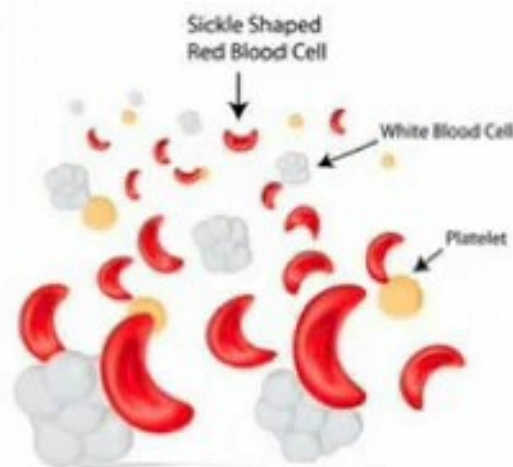
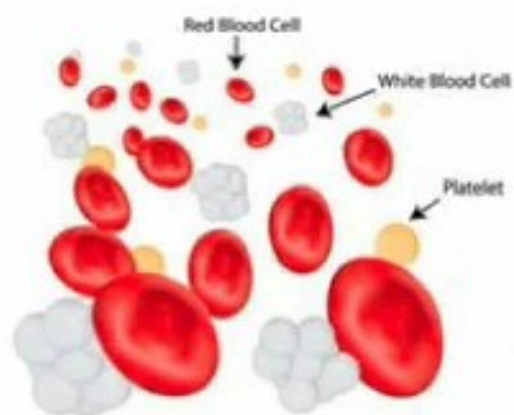
- ① **Repeated Blood transfusions** to correct the anemia and to suppress the Bone Marrow and thus decrease the production of abnormal cells (to decrease hemolysis).
- ② Add **Desferoxamine** to the treatment to AVOID secondary hemochromatosis.
- ③ **/! Bone Marrow Transplantation**
- ④ **Hydroxyurea** to increase the production of Hemoglobin F

Hemolytic Anemia (Sickle Cell Anemia)



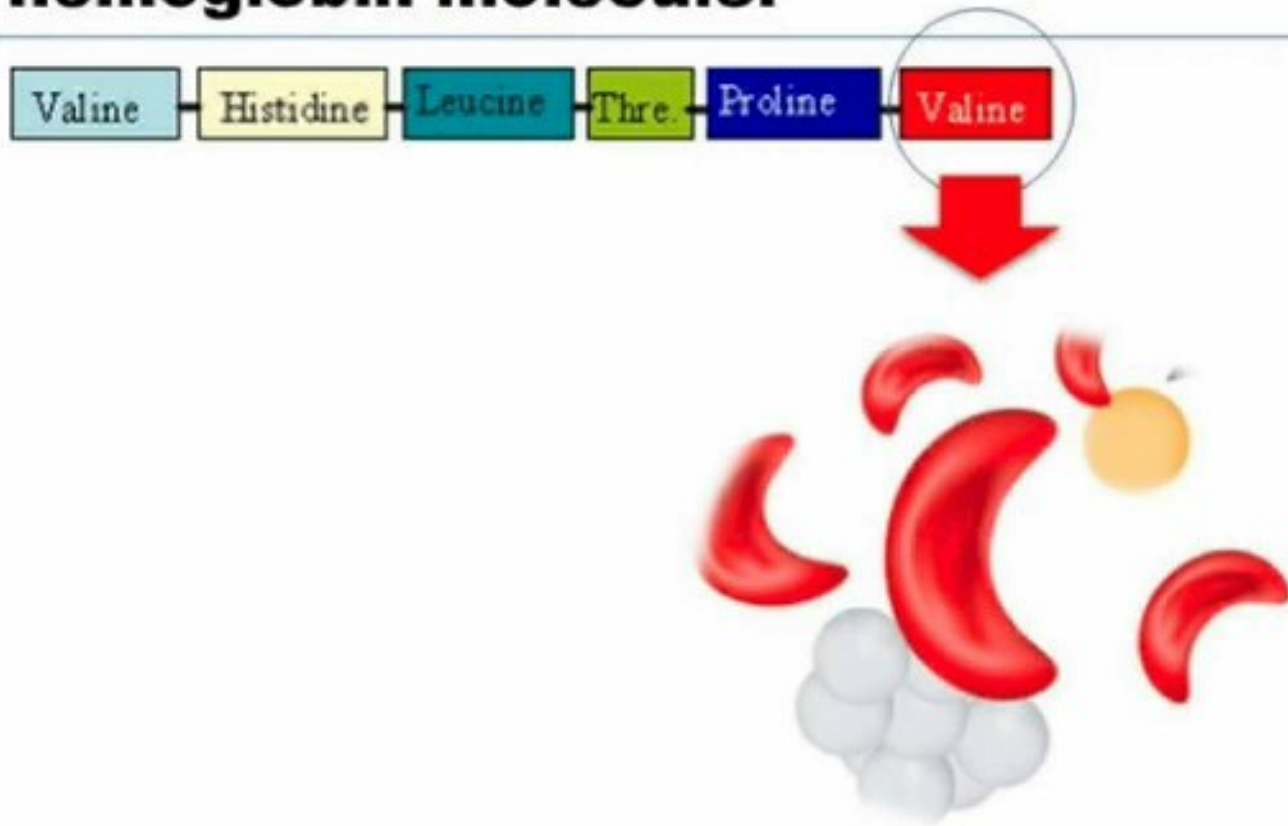
Definition

A form of hemolytic anemias characterized by the presence of **Hemoglobin S** instead of the normal adult hemoglobin or (Hemoglobin A)



Aetiology

A single base mutation in the DNA causing the presence of **Valine instead of Glutamic acid** in position **Number 6** of the beta chains of the hemoglobin molecule.



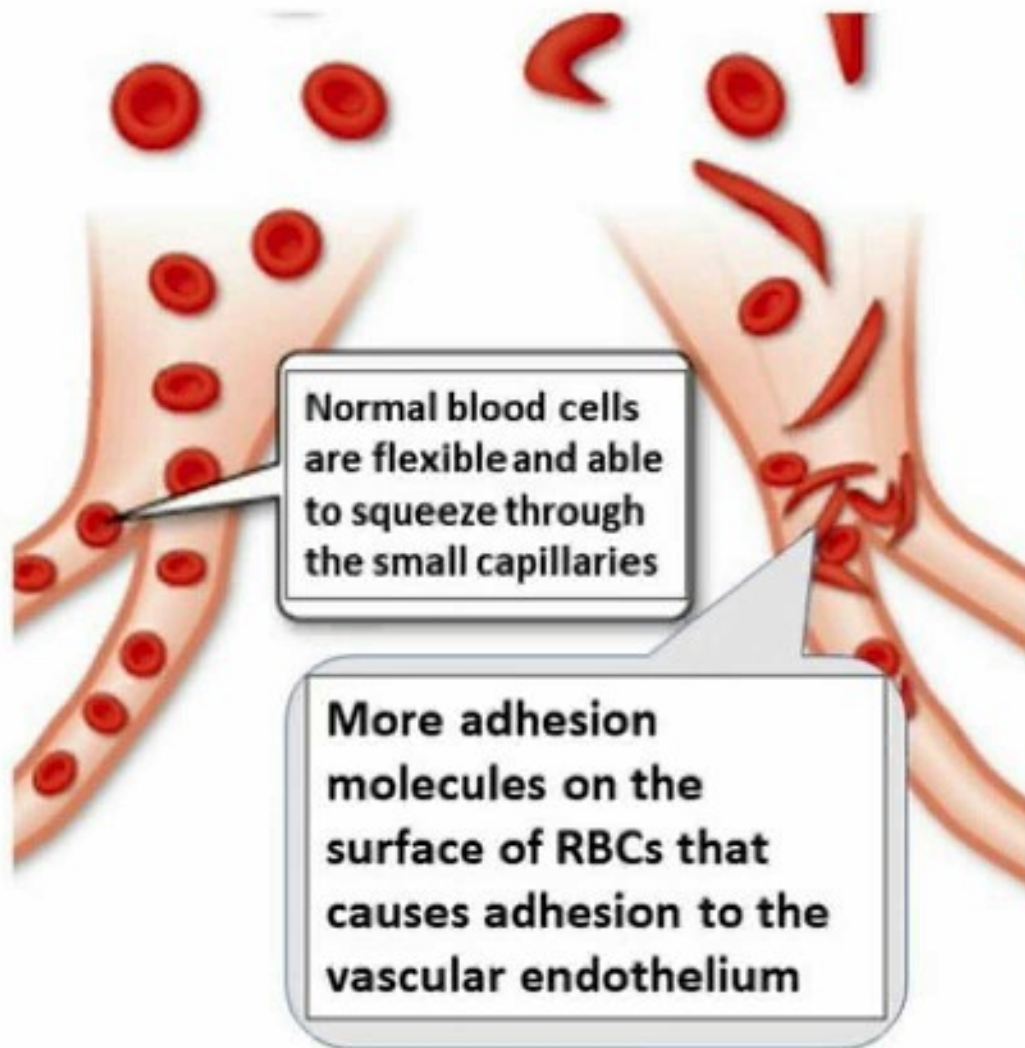
Mechanism

Low Oxygen tension
Hemoglobin S undergoes
aggregation and
polymerization causing the
red cells to be rigid and
deformed.



**Sickle Cell
Shape**

Mechanism



Micro-infarcts



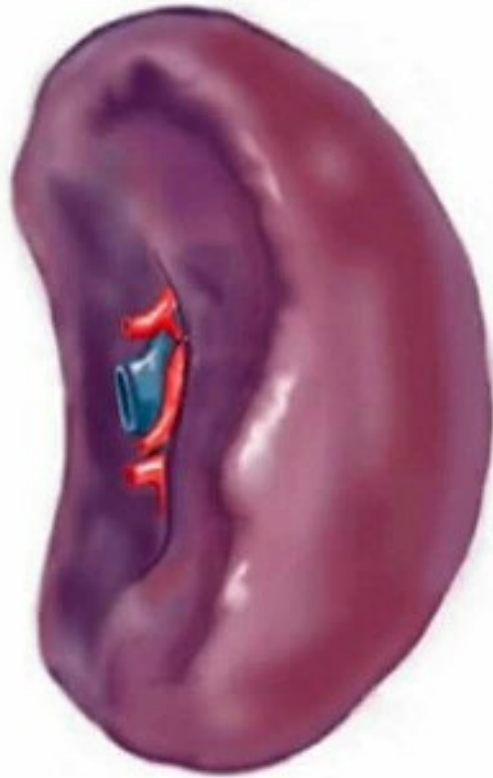
Vascular occlusion Crisis



Bones-Kidney
Skin- Cerebral vessels
Retina-Mesenteric
vessels

Mechanism

Sequestration
in Splenic
sinusoids



**Hemolytic
anemia**

Micro infarcts



Tissue
necrosis



Fever



Autosplenectomy



Infections:
Pneumococcal
pneumonia
Septicemia



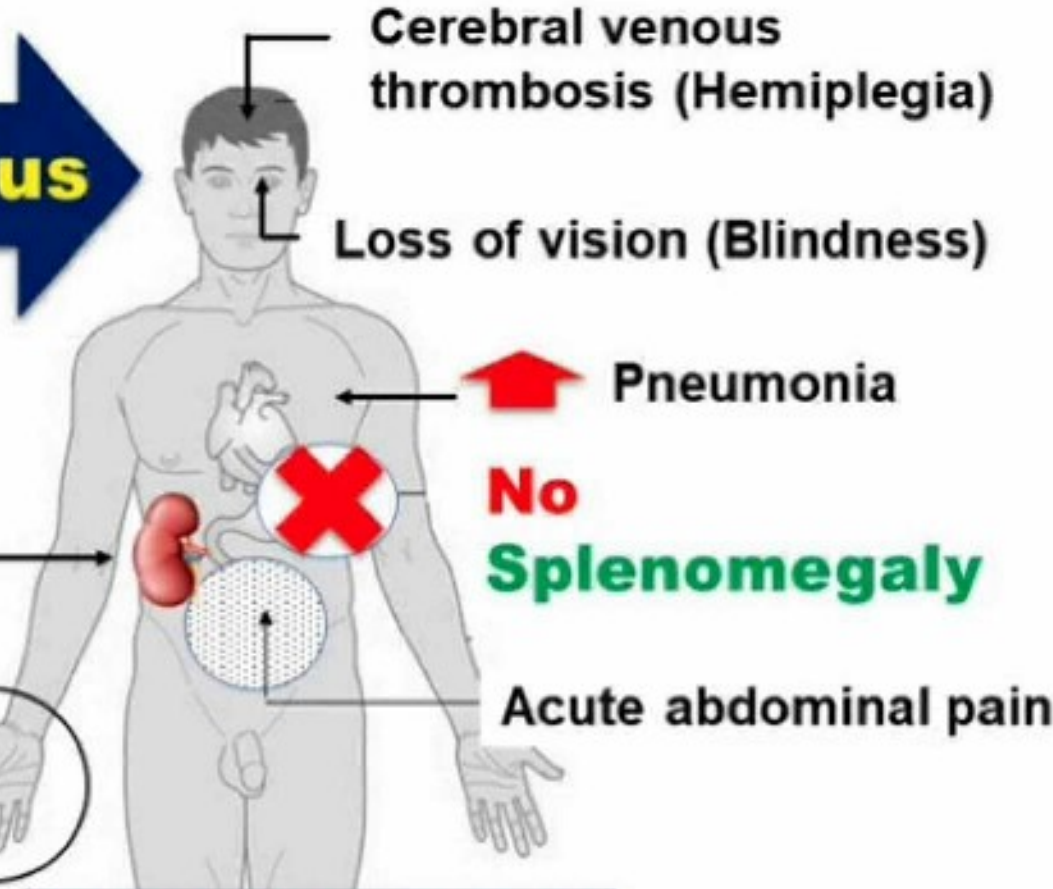
Bones



Osteomyelitis
(Staph &
Salmonella)

Clinical Picture

General features of hemolysis



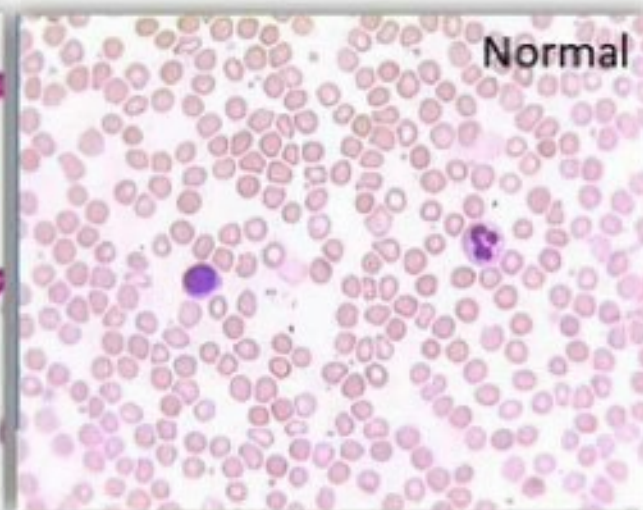
Precipitating Factors
Exercise- Fever-
Emotional Stress



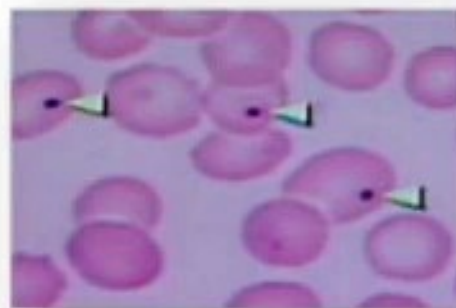
Sickle Cell Crisis

Special Investigations

Sickle Cells



Howell-Jolly bodies and Target cells



Hemoglobin S

Features of hemolysis

Treatment

No specific treatment is available, however, the following should be done:

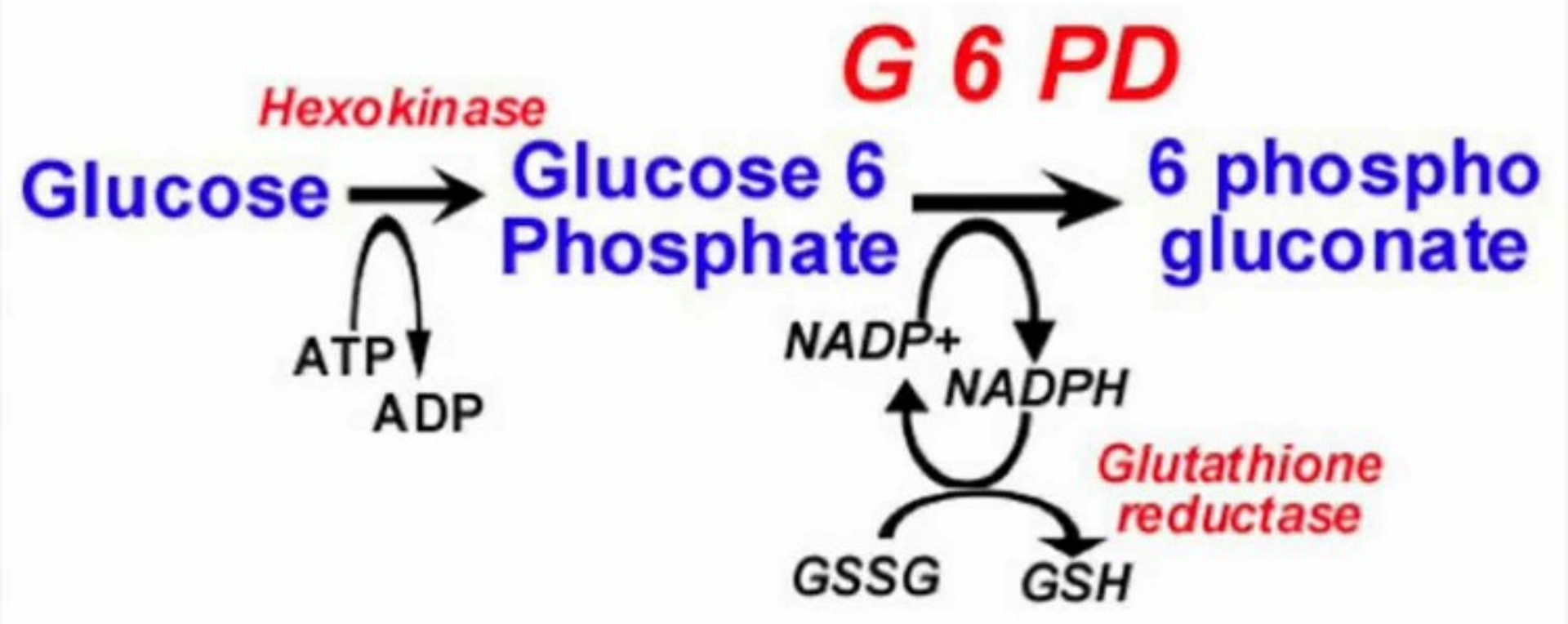
- ① Repeated Eye examination to check the retina
- ② Vaccination against pneumonia and Influenza
- ③ Folic acid
- ④ Antibiotic prophylaxis against pneumonia e.g. Penicillin
- ⑤ Avoid dehydration as it may precipitate vasoocclusive crisis.

Treatment

Treatment of the Vasoocclusive Crisis

- 1 Proper Hydration**
- 2 Intranasal Oxygen**
- 3 Aggressive narcotic analgesia**
- 4 Hydroxyurea- it increases Hemoglobin F inside the RBCs thus decreases sickling of cells.**
- 5 Treatment of underlying precipitating factors e.g. infections**

Hemolytic Anemia (G6PD Deficiency)



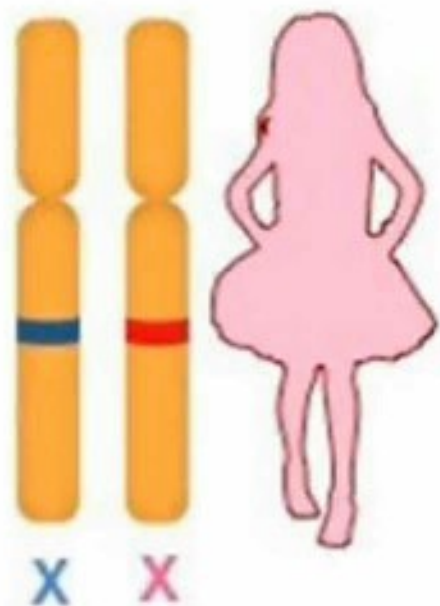
Definition

G6PD deficiency is an inherited enzymatic defect that causes episodic hemolysis in response to exposure to oxidative stress.

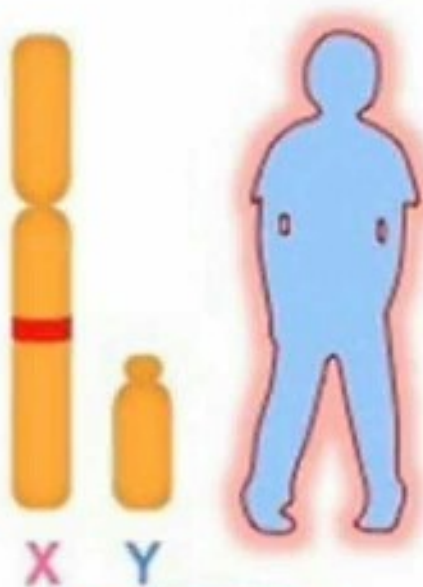
- ① Infections
- ② Drugs
- ③ Fava beans
(Favism)



Hemolysis



Normal - *carrier*



Affected

Mechanism



G6PD



NADPH



**Reduced
Glutathione**



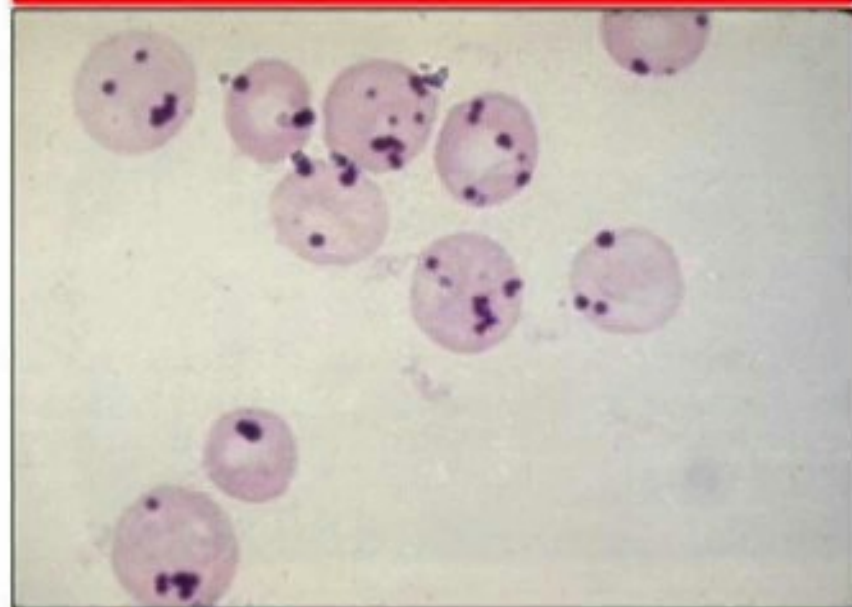
**Increased
Susceptibility to
Oxidative Damage**

Mechanism

Oxidative damage may cause oxidation of hemoglobin and its ppt as Heinz bodies inside the affected cells



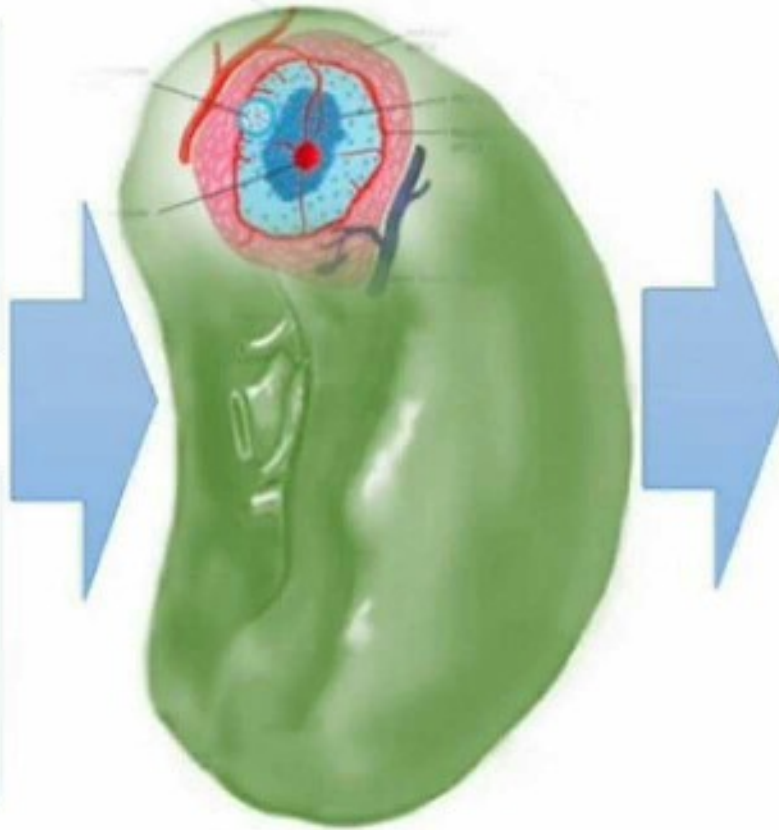
Heinz bodies



Mechanism

Heinz bodies
causes
membrane
damage.

The affected
cells are
removed by
the spleen



**Hemolytic
anemia**

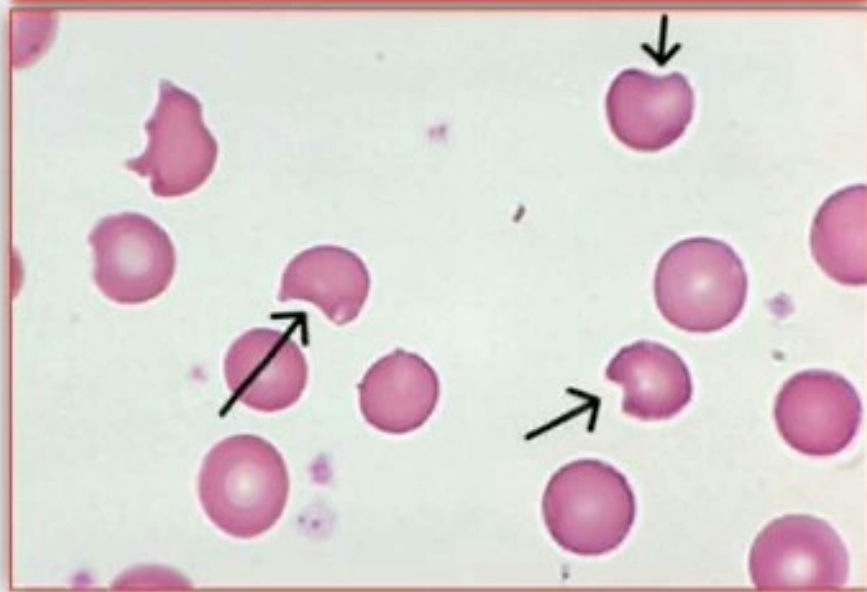
Anemia
Increase Indirect
Bilirubin
Reticulocytosis

Mechanism

Splenic
macrophages try to
plunk out the Heinz
bodies



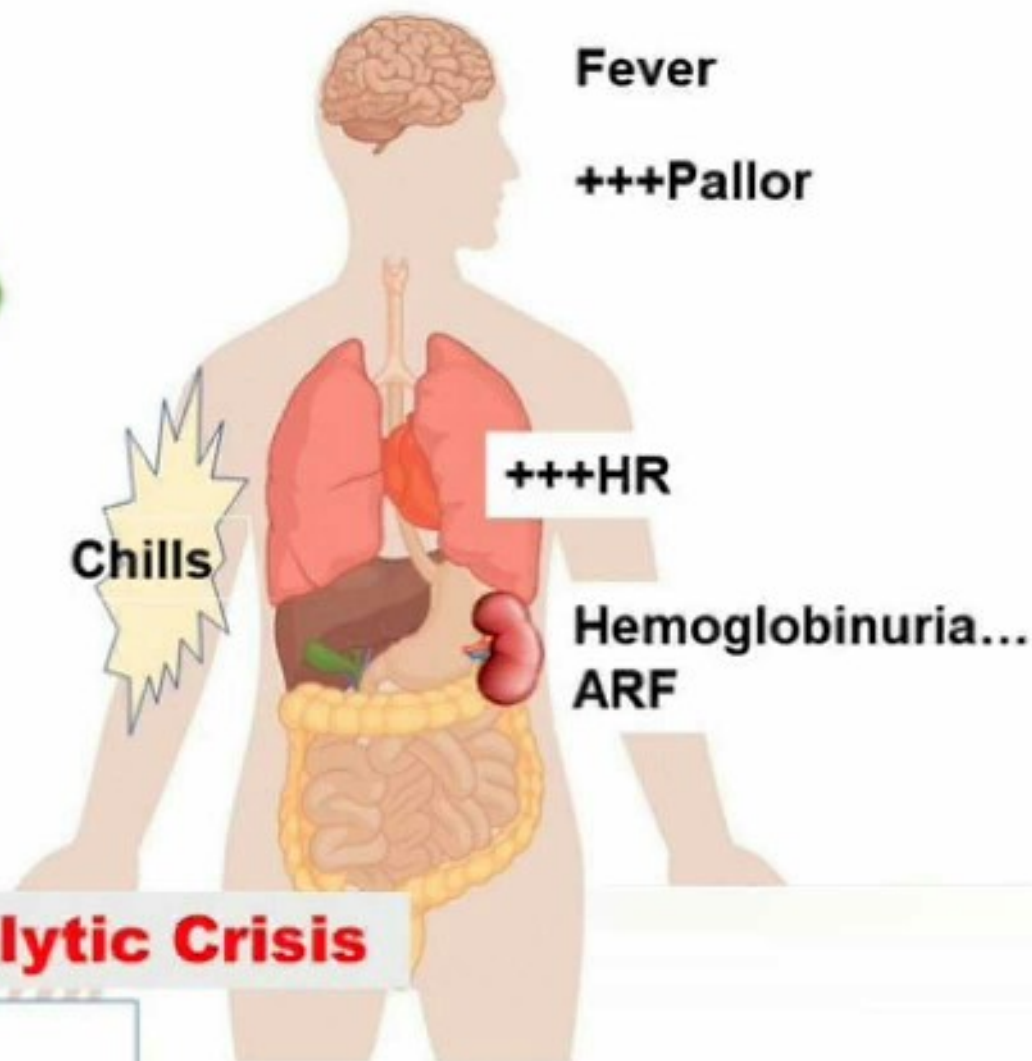
Bite Cells



Clinical Picture

Oxidative damage

- ① Infections
- ② Drugs
- ③ Fava beans
(**Favism**)



Acute Hemolytic Crisis

Drugs

Dapsone
Primaquine
Quinine
Sulpha
Nitrofurantoin

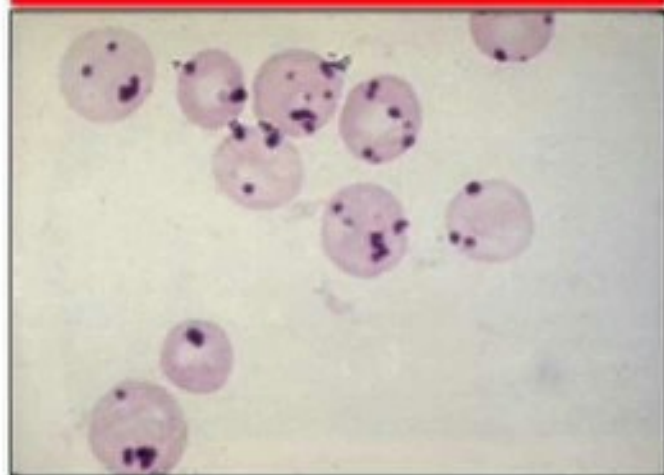
Special Investigations

Low G6PD activity

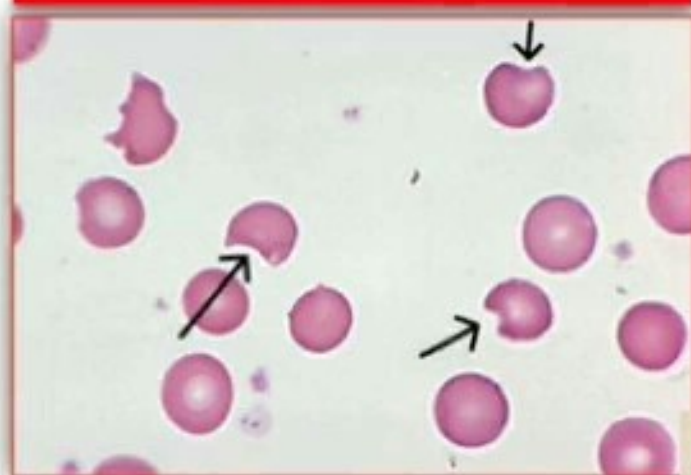


Measure it AFTER the attack as it can be normal during the attack

Heinz bodies



Bite Cells



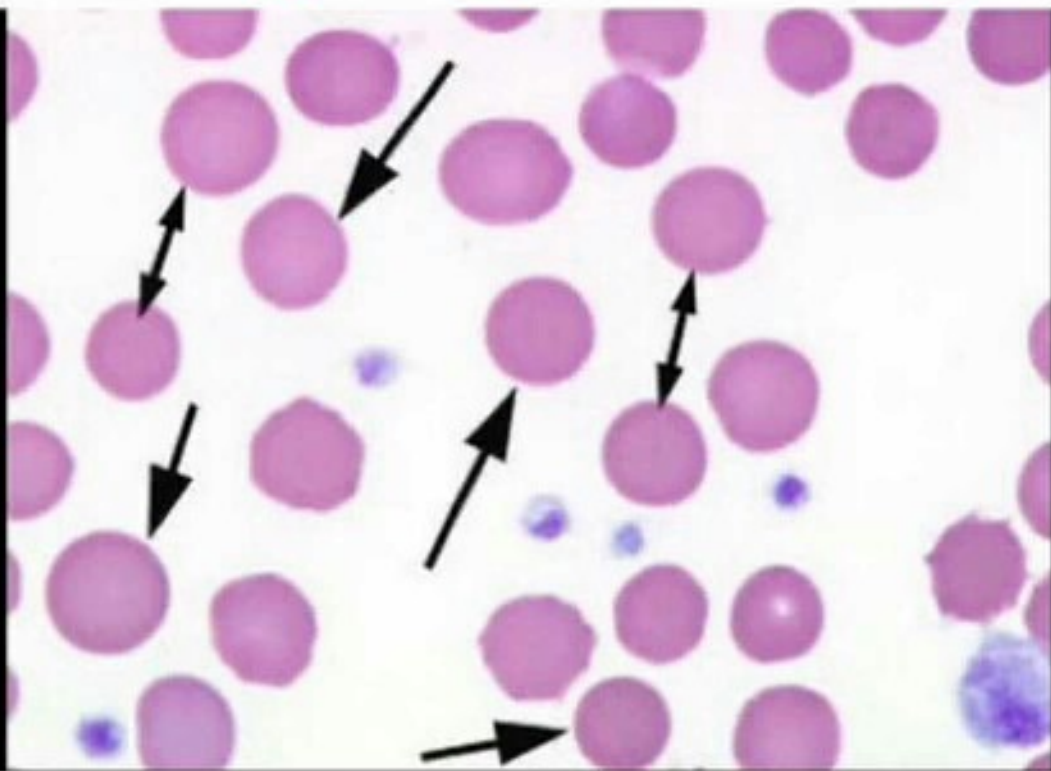
Treatment

AVOID any ppt factor for the attacks

Treatment of Acute Hemolytic Crisis include:

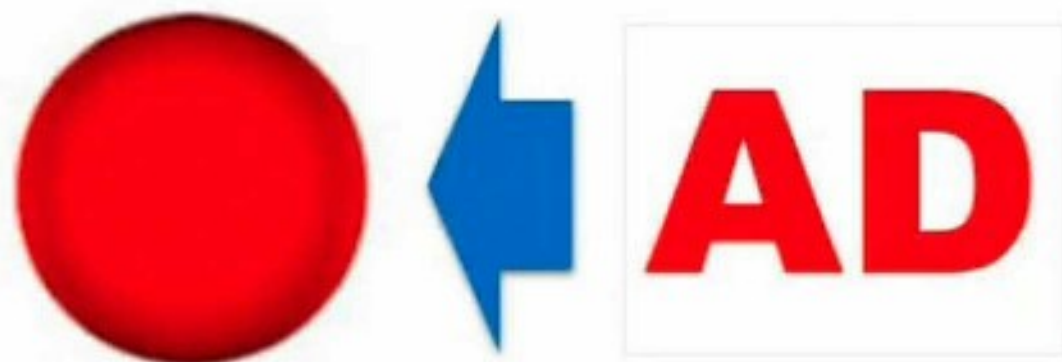
- 1 Corticosteroids**
- 2 Alkaline Urine**
- 3 Blood transfusion**

Hemolytic Anemia (Hereditary Spherocytosis)



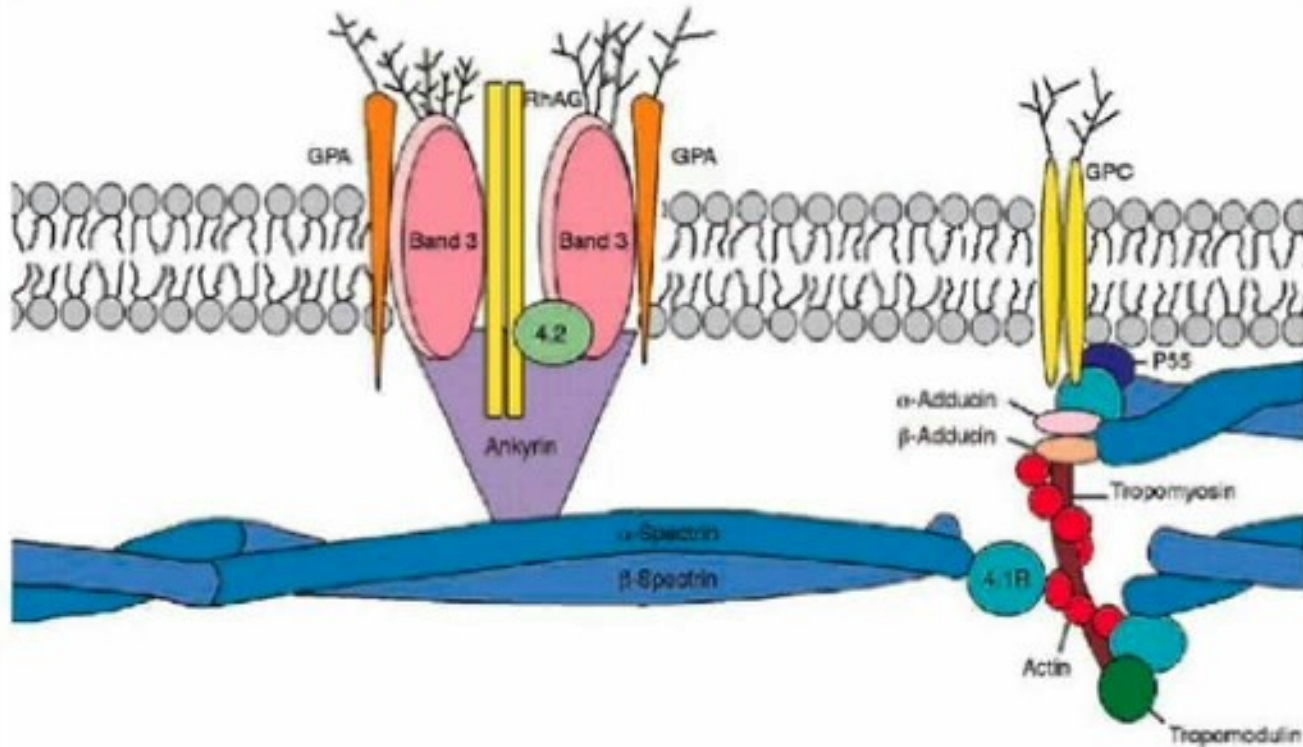
Definition

An Autosomal Dominant (AD) disorder characterized by the presence of “Spherical” RBCs called Spherocytes instead of the normal ‘biconcave’ ones.



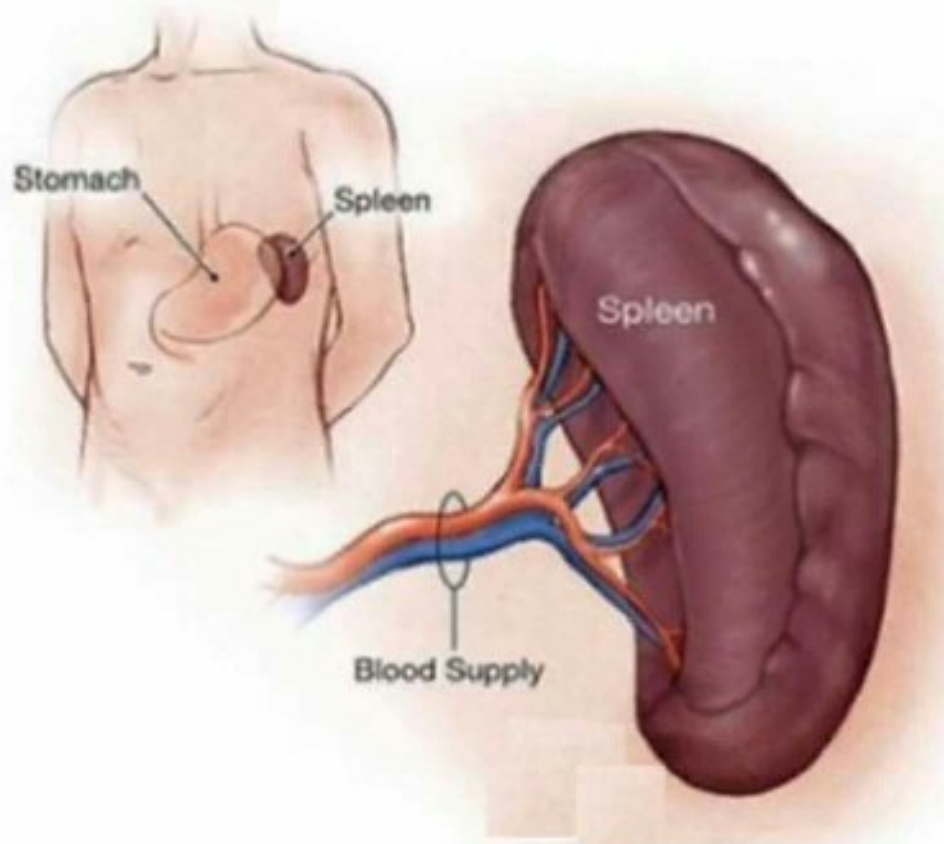
Aetiology

A defect in a Cytoskeleton protein called **Spectrin**.
This defect makes the RBCs spherical and decreases their 'deformability'.



Mechanism

Role of the Spleen



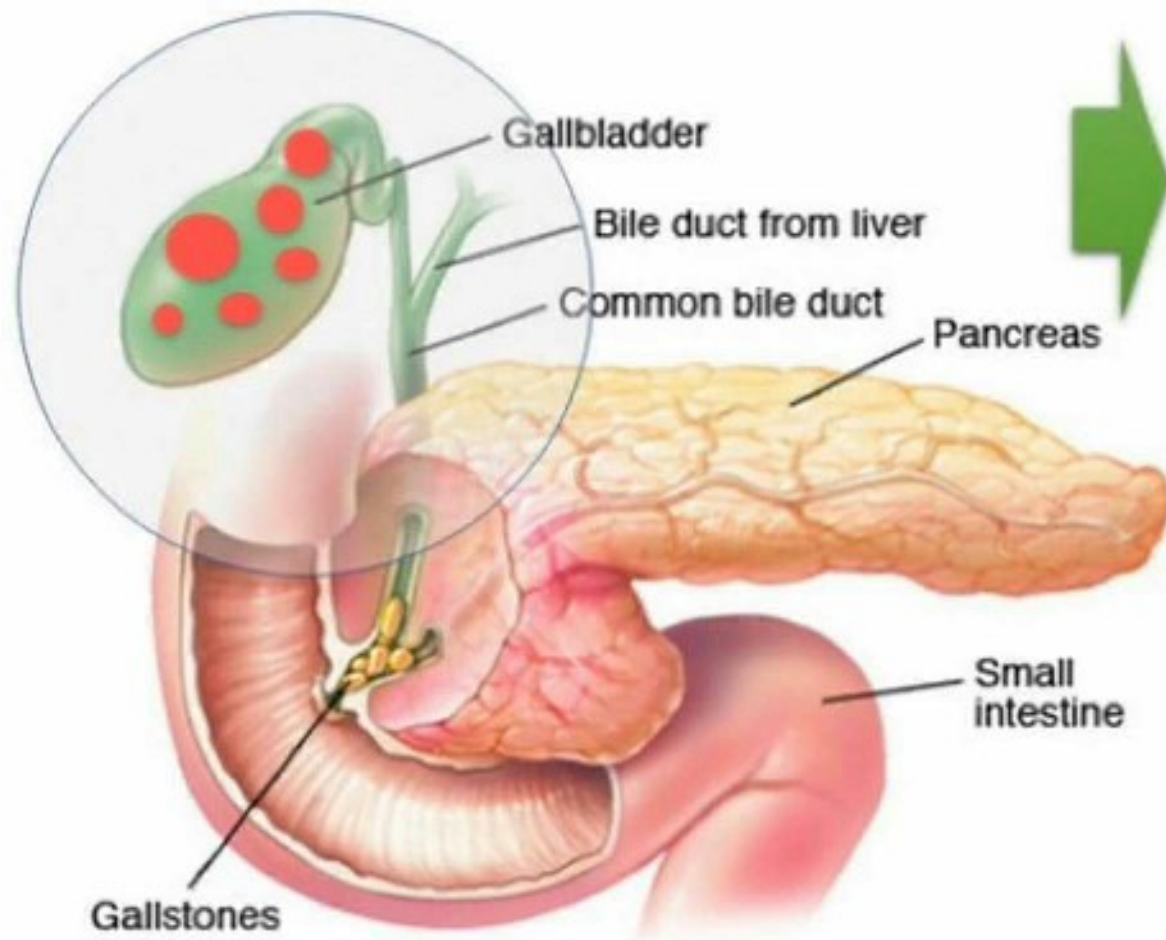
**Associated
with massive
Splénomegaly**

**Treatment by
Splenectomy**

**Hemolysis in
the spleen**

Mechanism

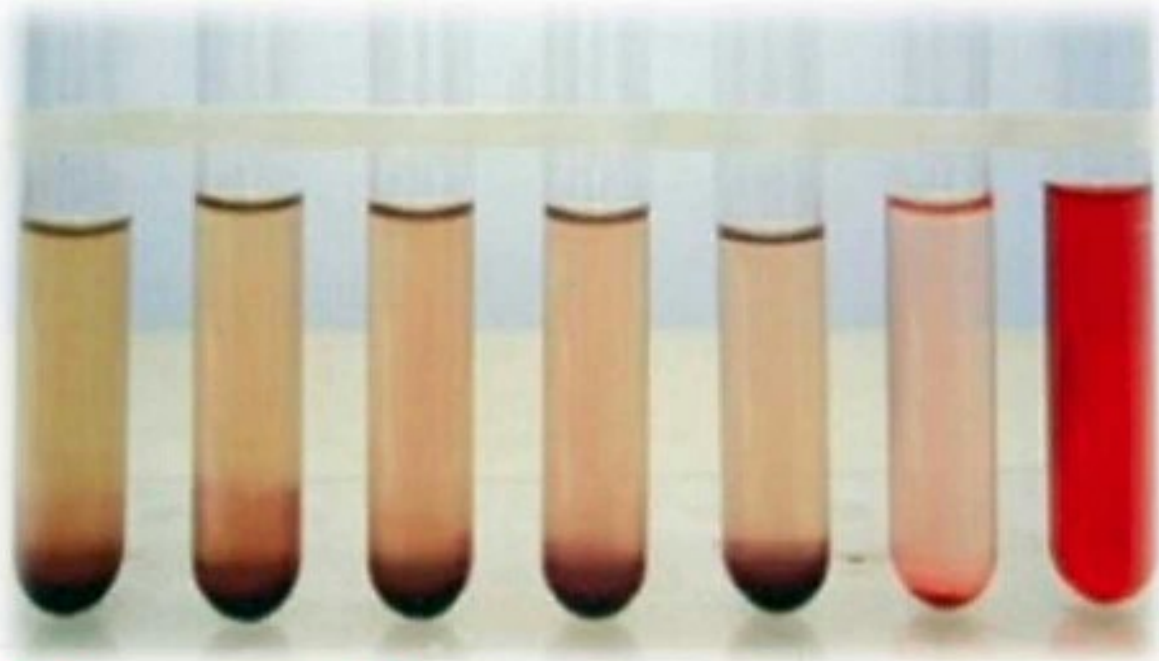
Gall bladder Stones



**Associated
with Gall
Bladder Stones**

Mechanism

↑ Osmotic Fragility



Osmotic Fragility Test

Vertigo

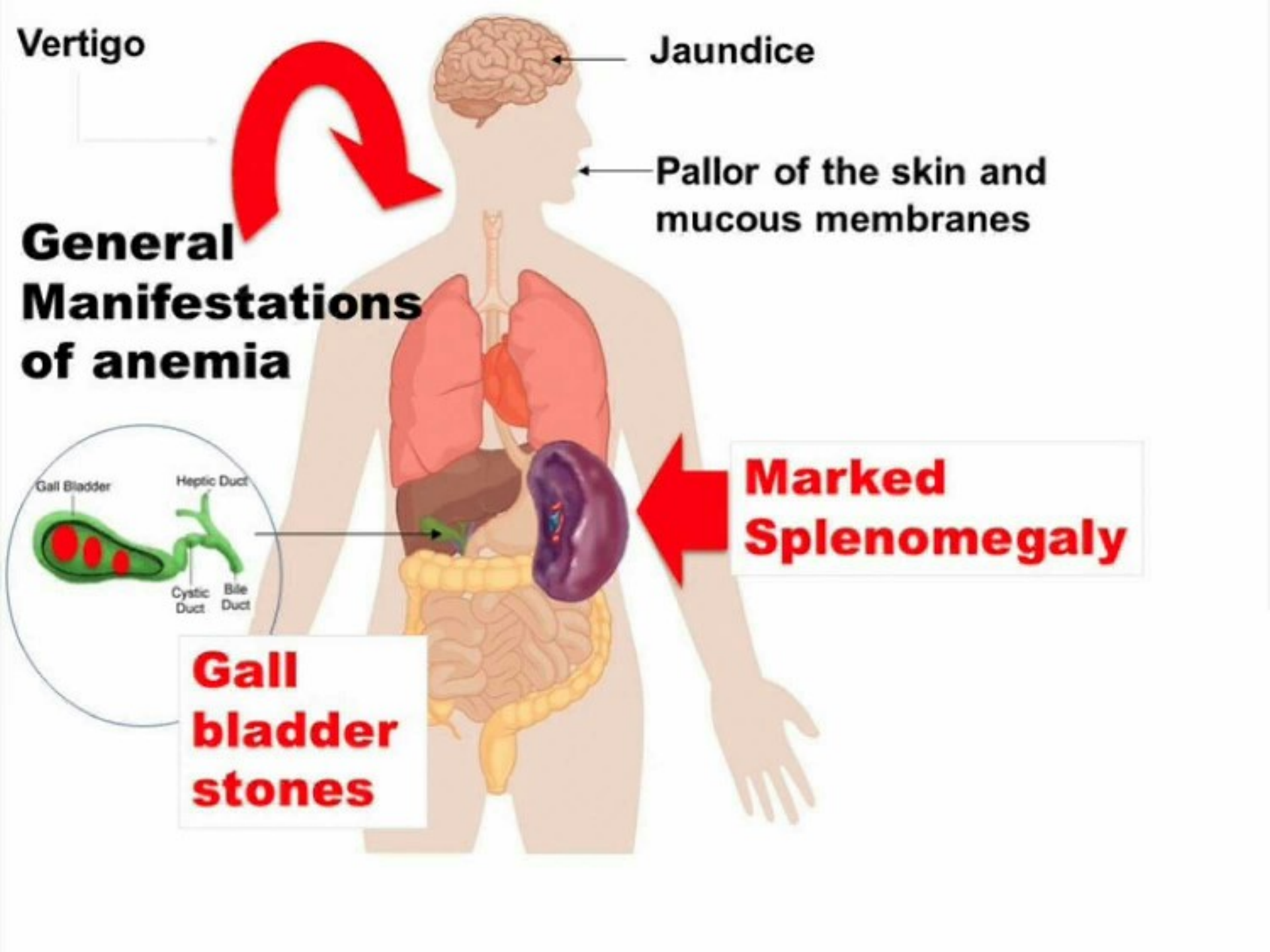
Jaundice

Pallor of the skin and
mucous membranes

**General
Manifestations
of anemia**

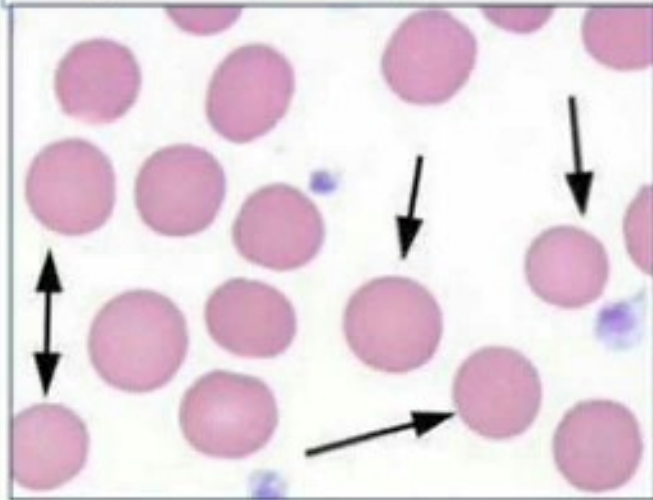
**Marked
Splenomegaly**

**Gall
bladder
stones**



Special Investigations

Spherocytes

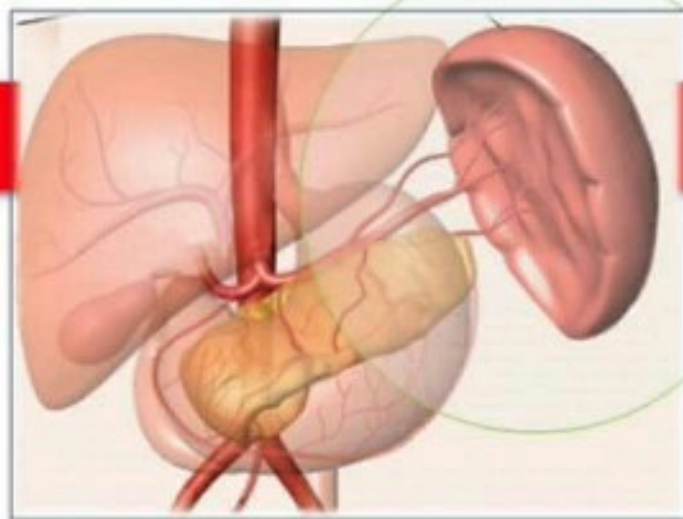


**Osmotic
Fragility**

**Negative
Coombs Test**

Treatment

Splenectomy



Hemolytic Anemia

Paroxysmal Nocturnal Hemoglobinuria

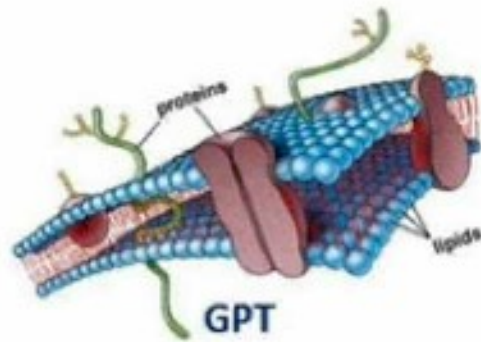


Definition

PNH is a condition associated with increased sensitivity of RBCs membrane to lysis by alternative complement pathway.

Aetiology

The basic defect in PNH is deficiency of membrane linked proteins that normally regulate complement activity (these proteins include: DAF, CD 55, CD59)



Membrane become sensitive to lysis by alternative complement pathway



RBCs



WBCs



Platelets



Mechanism

Sleep



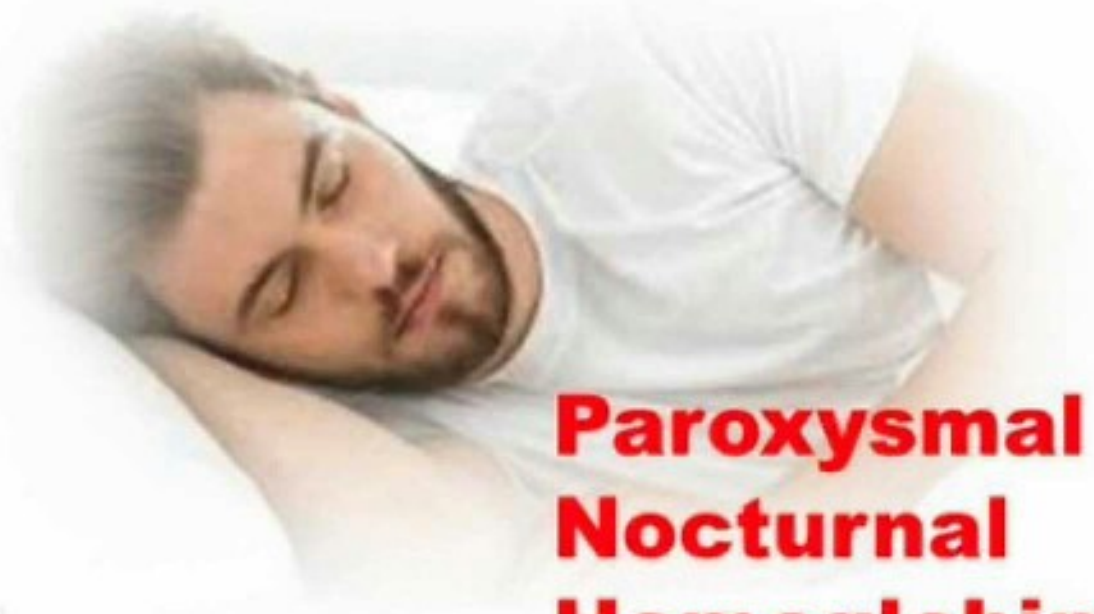
'mild'
acidosis'



Alternative
complement
pathway



Attacks



**Paroxysmal
Nocturnal
Hemoglobinuria**

Mechanism

Liberation of thrombogenic substances from the lysed cells may cause thrombosis in different parts of the body (**Hypercoagulability**)

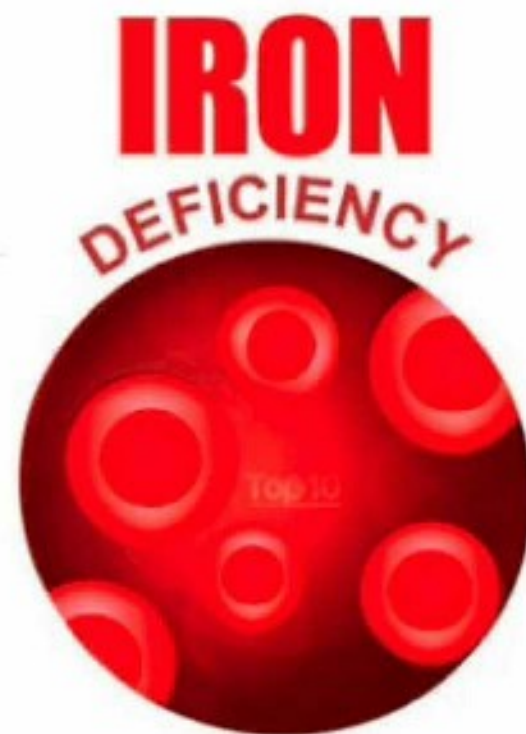
Examples:

Mesenteric venous thrombosis
Hepatic venous thrombosis
cerebral venous thrombosis



Mechanism

Chronic hemolysis my cause
Hemosiderinuria which may lead
to the development of **IDA**



Clinical Picture
Recurrent
Attacks
During Sleep

Cerebral
Venous
Thrombosis

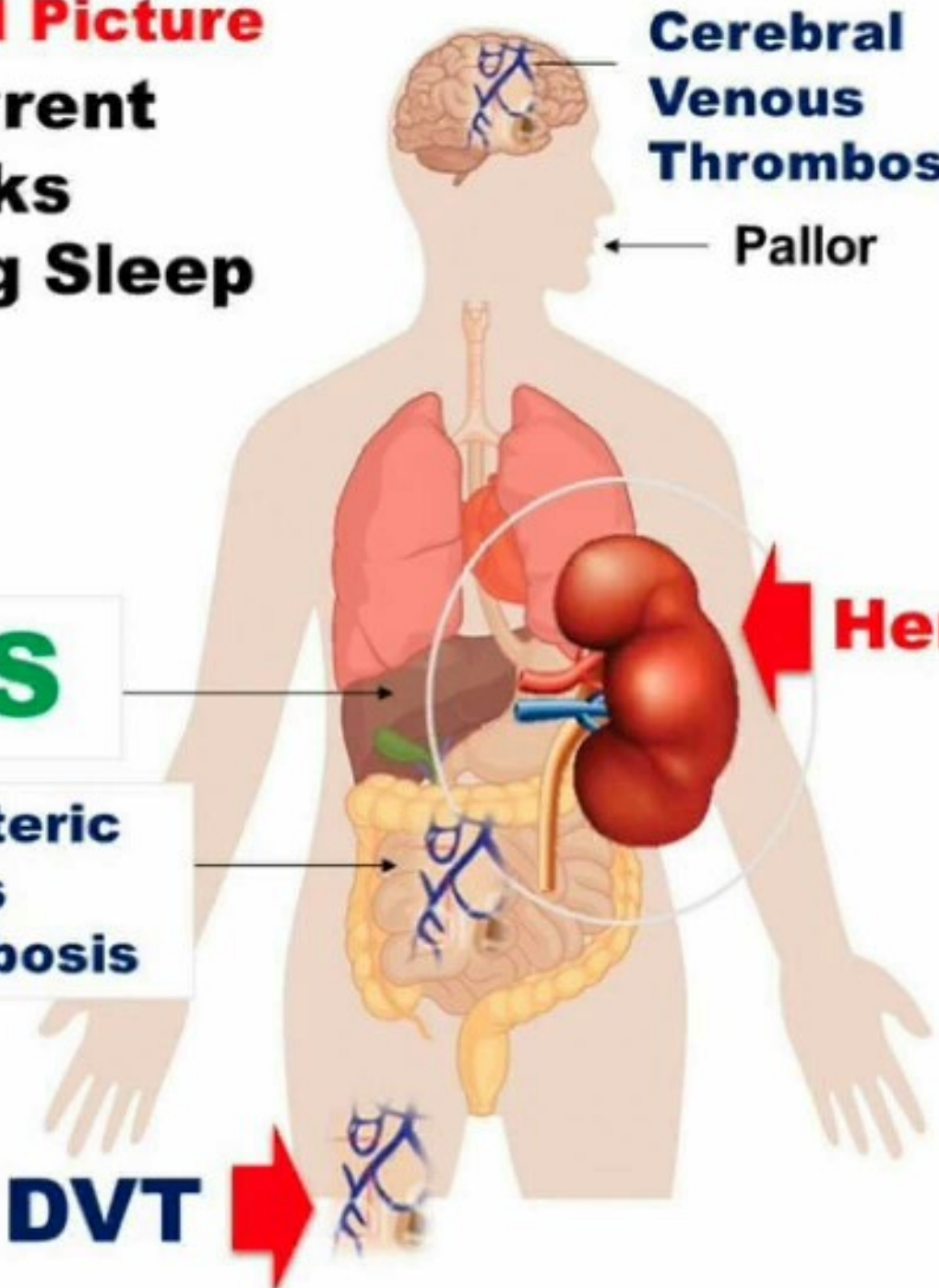
Pallor

BCS

Mesenteric
Venous
Thrombosis

Hemoglobinuria

DVT



Special Investigations

PCP

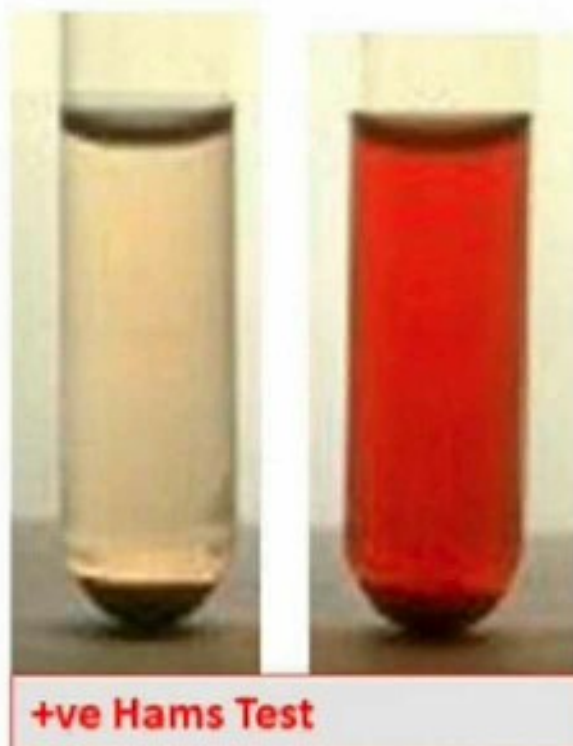
Hemosiderinuria

**+ve Hams Test
OR/ +ve Sucrose
Test**



LDH

**Absent CD59 by
Flow cytometer**



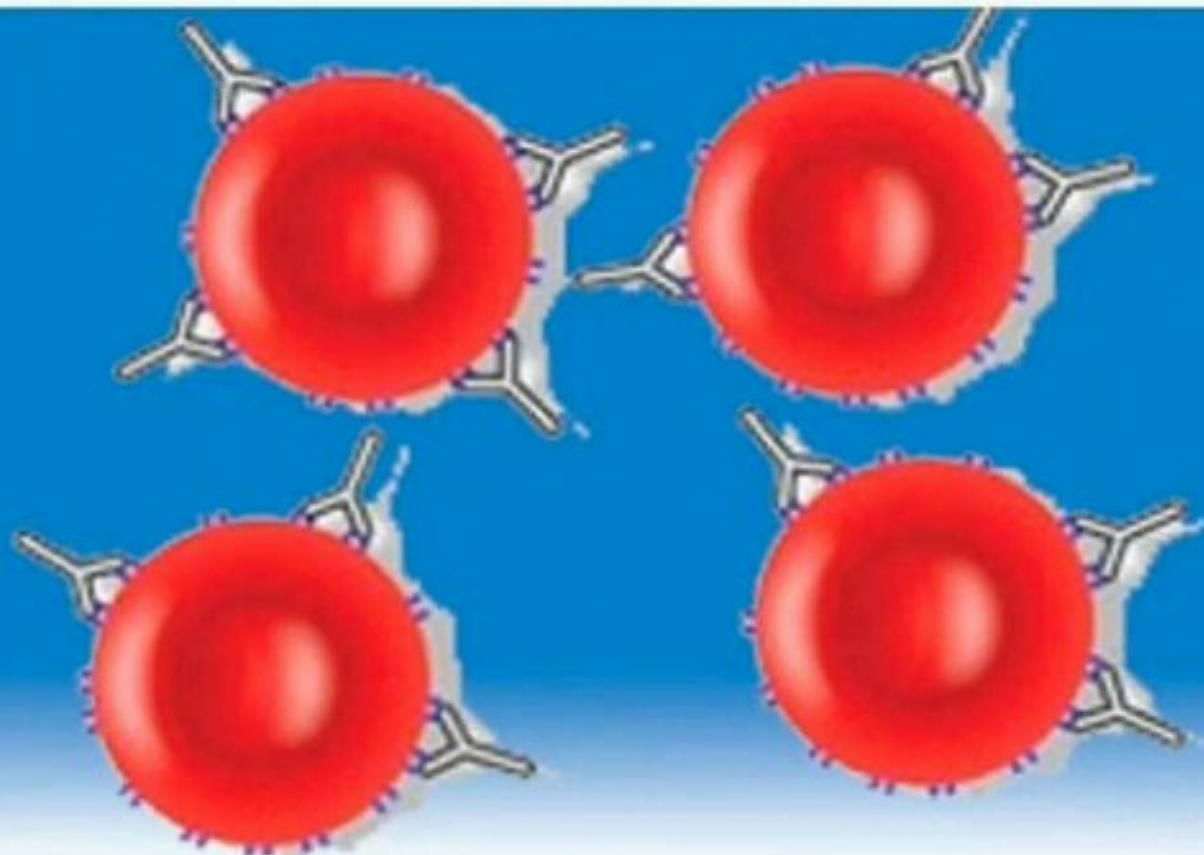
Treatment

- ① Blood transfusion to decrease hypoxia and thus decreases the proliferation of the abnormal clone cells.
- ② Prednisone to diminish hemolysis
- ③ Iron treatment for associated IDA (**Note**: Iron therapy may initiate the attacks of hemolysis due to formation of new RBCs)
- ④ Heparin for thrombotic episodes

Complement inhibition by **Eculizumab** is a promising new approach to treating the hemolytic anemia.

Hemolytic Anemia

Autoimmune Hemolytic Anemia



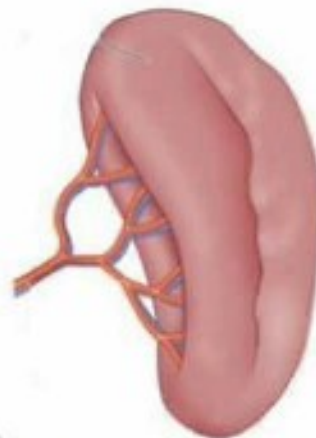
Definition

AIHA is an acquired disorder caused by immune antibodies against the RBCs.

Types

Hot Hemagglutinins **IgG**

IgG



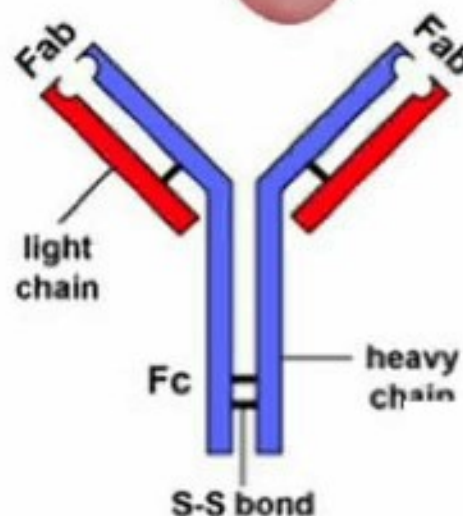
Hemolysis occur in the Spleen

RBCs destroyed by **Splenic Macrophages** (Fc Receptors)

Splenic macrophages removes the coated RBCs thus may remove parts of the cell membrane creating **Spherocytes**.

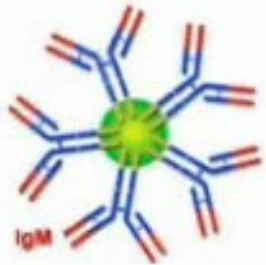
Causes:

- 1 Idiopathic (50%)
- 2 SLE
- 3 CLL
- 4 Lymphomas



Types

Cold Hemagglutinins IgM



Hemolysis occur in cold exposed areas such as: **Fingers- Nose- Ears**. Numbness of fingers on exposure to cold.

IgM can fix complement causing destruction in the **Liver** as well. This occurs via complement activation process that involves removal of RBCs by VKCs in the Liver via **C3b Receptors**.

Causes:

- ① Mycoplasma Pneumonia
- ② IMN
- ③ Idiopathic

Clinical Picture

Hot Hemagglutinins IgG

Hemolysis

Anemia

Splenomegaly

Cold Hemagglutinins IgM



Special Investigations

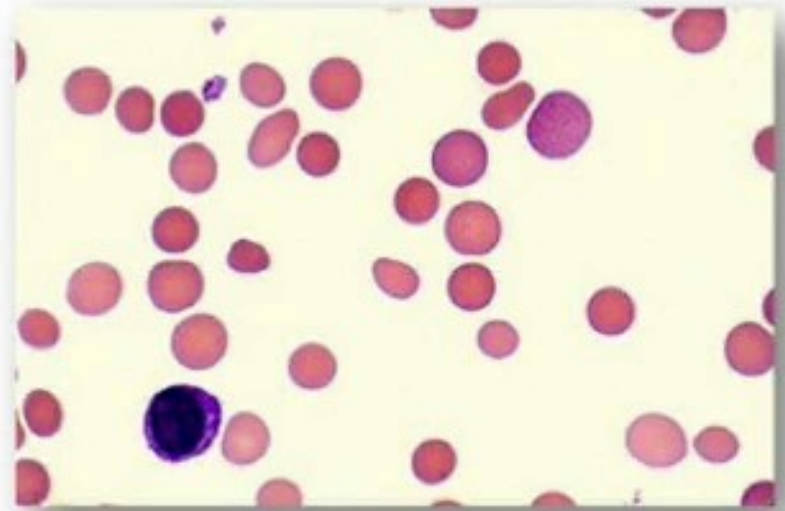
Hot Hemagglutinins **IgG**

Spherocytes

Hemolysis

Increased Indirect Bilirubin
Reticulocytosis
Decreased hematocrit

+ve Coombs test



Cold Hemagglutinins **IgM**

**+ve Cold
agglutinin test**



Treatment

Hot Hemagglutinins **IgG**

- 1 Corticosteroids
- 2 Splenectomy
- 3 Immunosuppressive drugs
- 4 High dose IV Immunoglobulins to saturate the Fc Receptors on the Macrophages and thus decreases hemolysis

Cold Hemagglutinins **IgM**

- 1 **Avoid exposure to Cold**
- 2 Steroids and Splenectomy?!
- 3 Immunosuppressive drugs may be useful in some cases

Bleeding Tendency **(Introduction)**



① Blood Vessels



Bleeding Time

② Platelets



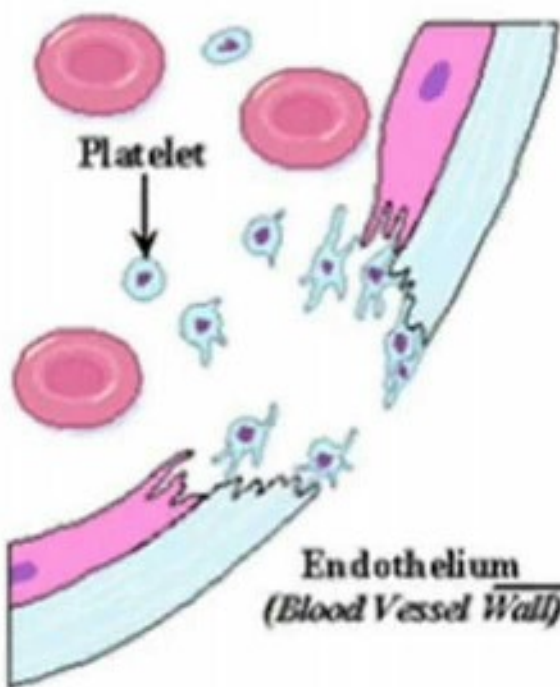
Bleeding Time

③ Coagulation Process

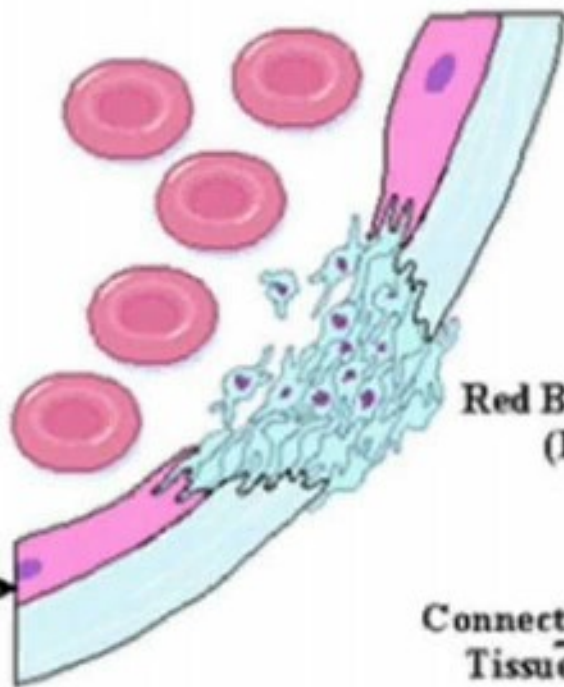
Coagulation Time



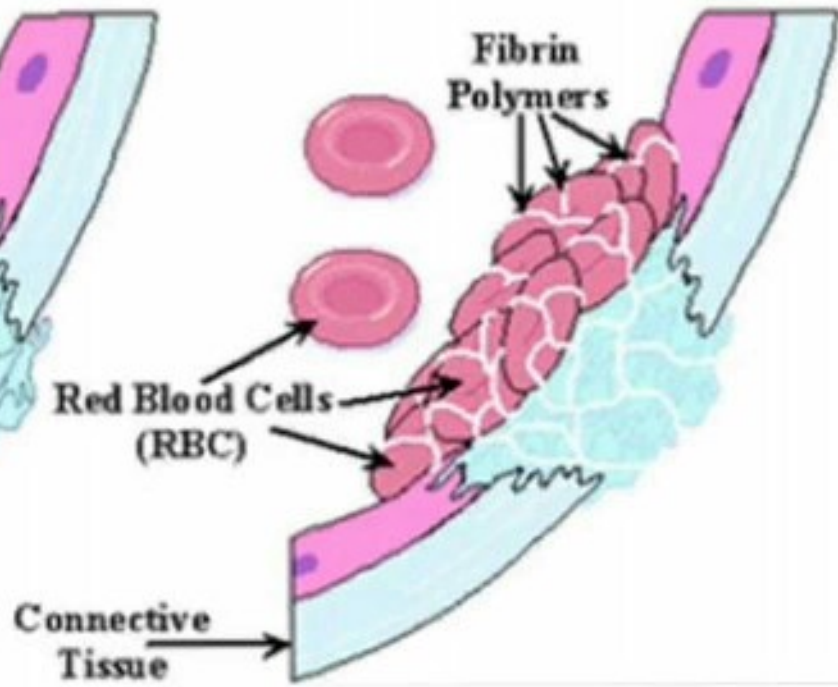
Platelet adherence



Release of Mediators



Fibrin deposition



Contact activation

Tissue factor

intrinsic

extrinsic

XII

XI

IX

VIII

VII

common

X

V

II

fibrinogen

Fibrin

Partial thromboplastin time
aPTT
heparin

Prothrombin time
PT
warfarin

Causes

Purpura

Coagulopathy

 **Bleeding Time**

 **Coagulation Time**

 **Platelet Count**

Thrombocytopenia

 **Platelet Functions**

Thrombocytopathy

Defect in blood vessels

Vascular Purpura

- ① Vitamin K Deficiency
- ② Hemophilia A
- ③ Von Willebrand Disease (**vWD**)
- ④ DIC

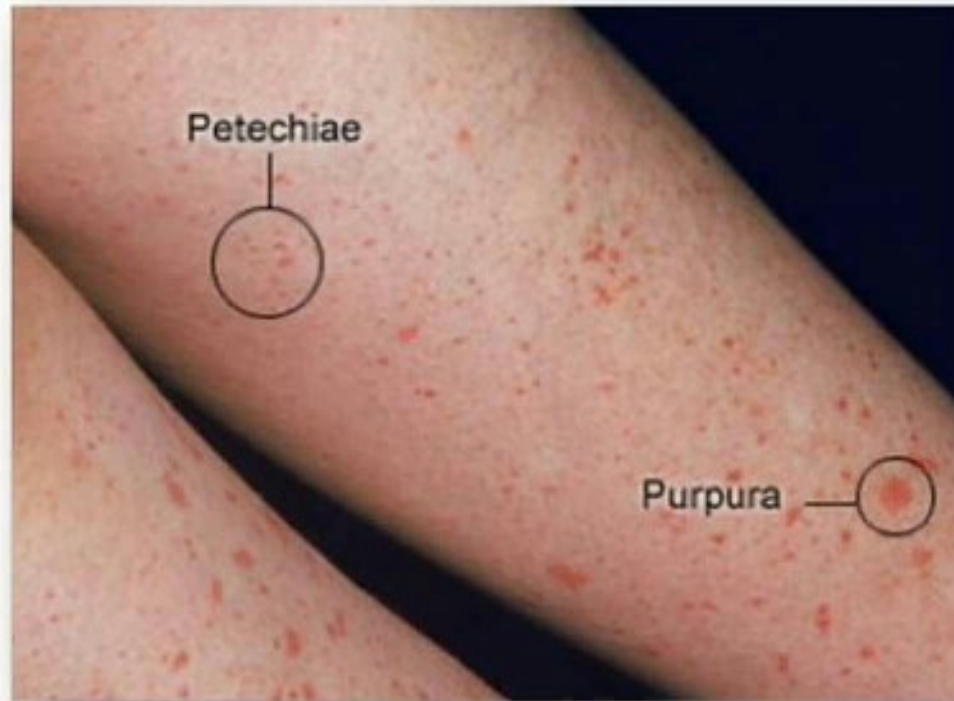
Bleeding Tendency

(Purpura: General)



Definition

Spontaneous bleeding in the form of Petechiae.



**Bleeding
Time**

Types



Platelet Count

Thrombocytopenia



1 Diminished production

Aplastic anemia
BM infiltration
Megaloblastic anemia
Some infections

2 Increased destruction

Idiopathic Thrombocytopenic
Purpura (ITP)
Drugs: Digoxin
Hypersplenism
DIC
SLE
PNH

Types



Platelet Functions

Thrombocytopathy



Causes

- 1- Idiopathic: Glanzmann's Disease (defect in platelet glycoproteins)
- 2- Drugs: Aspirin
- 3- CRF
- 4- LCF
- 5- Von Willebrand Disease (vWD)
- 6- Paraproteinemia (Hyperviscosity Syndrome)

Types

Defect in blood vessels

Vascular Purpura



Causes

- ① Allergic: Henoch- Schonlein purpura (HSP)
- ② Cushing Syndrome
- ③ CRF & LCF
- ④ Chemicals: Quinine- Penicillin- Chlorothiazide
- ⑤ Severe cough
- ⑥ Senility
- ⑦ Scurvy

Bleeding Tendency **(Coagulopathy: General)**

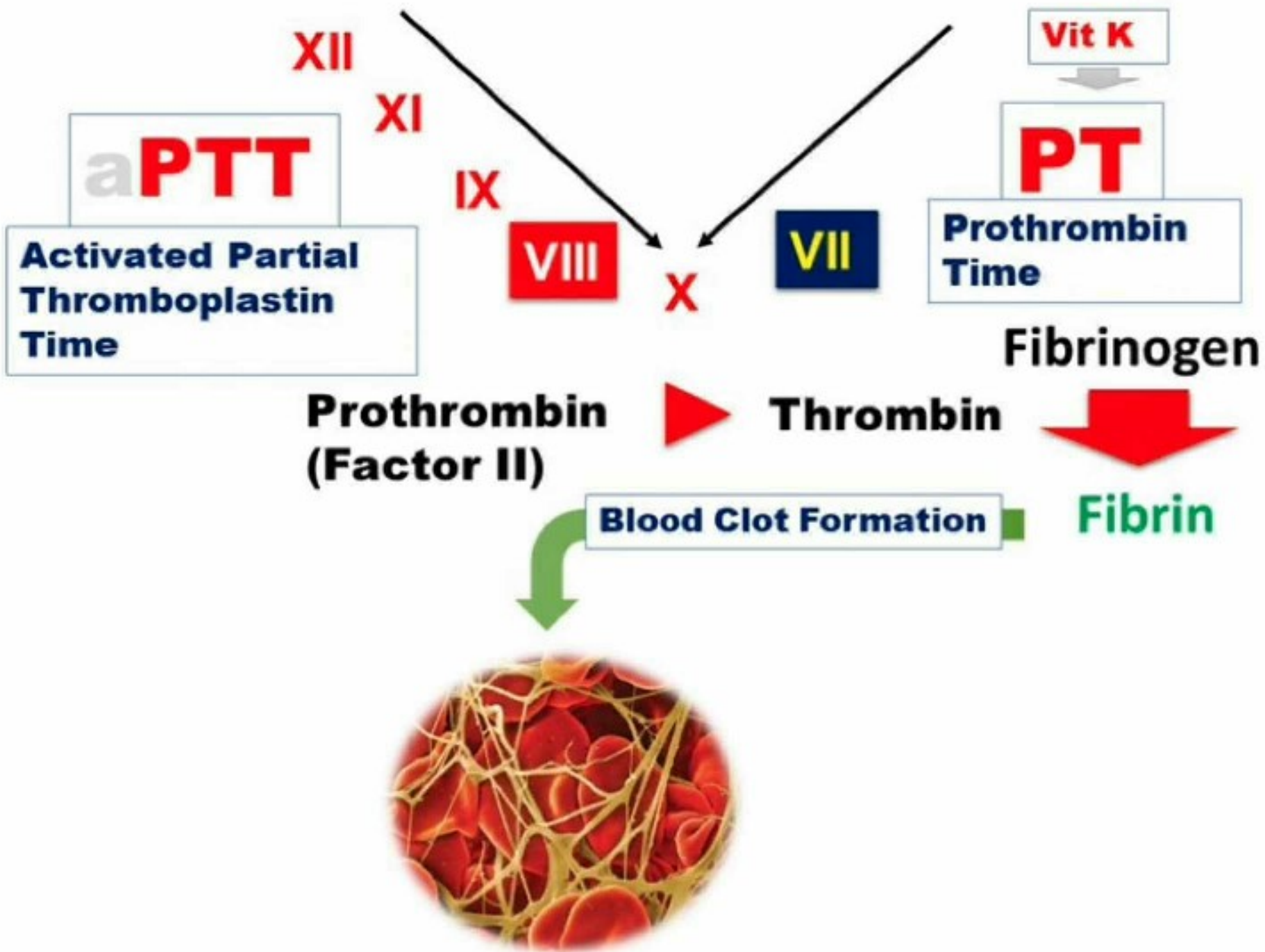


Definition

Bleeding every where due to defect in the coagulation system of the body. This could be due to either Quantitative or Qualitative defects of the Coagulation Factors.



**Coagulation
Time (s)**



Causes

Hemophilia A



PTT

- ① Mainly in Males
- ② Bleeding in Joints, Muscles, GIT is common
- ③ Spontaneous bleeding may occur
- ④ Low Factor VIII:C Coagulable activity
- ⑤ Normal Factor VIII Antigen

Causes

vWD

AD



PTT



**Bleeding
Time**

**Positive family
history**

Autosomal Dominant

Causes

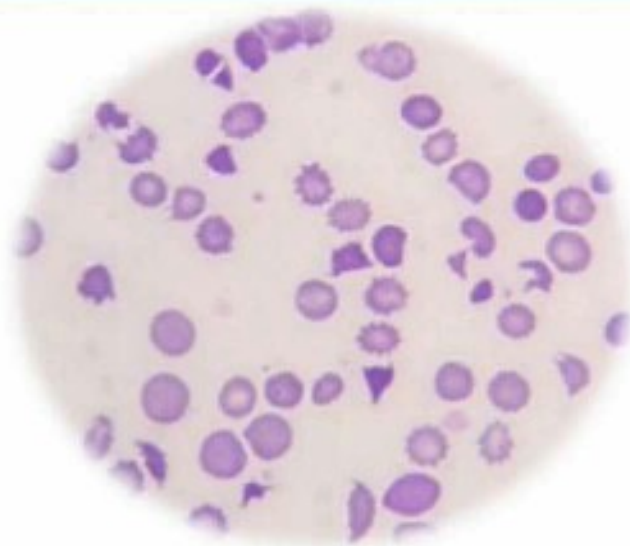
DIC



- 1 Underlying serious illness is usually present
- 2 Bleeding and Thrombosis occurs at the same time
- 3 Microangiopathic hemolytic anemia occurs in 25% of the cases (Fragmented RBCs)

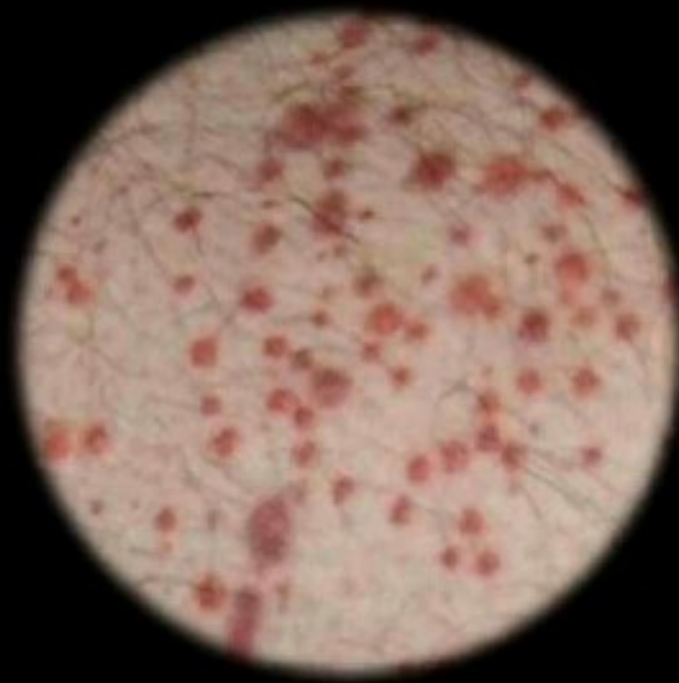


FDPs



Bleeding Tendency

Idiopathic Thrombocytopenic Purpura

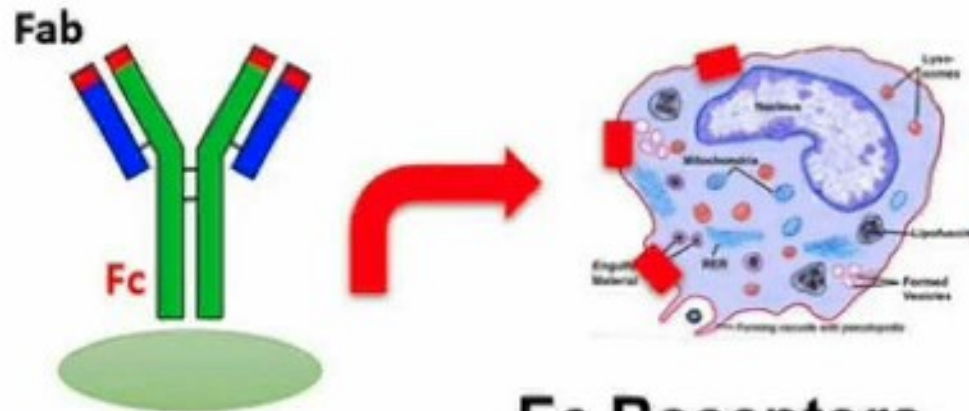


Definition

ITP is a hematological disorder characterized by immune mediated destruction of blood platelets.

Aetiology

IgG coated platelets are destroyed by the Splenic Macrophages.



Fc Receptors
of Splenic
Macrophages

Destruction
of blood
platelets

ITP

Clinical Picture

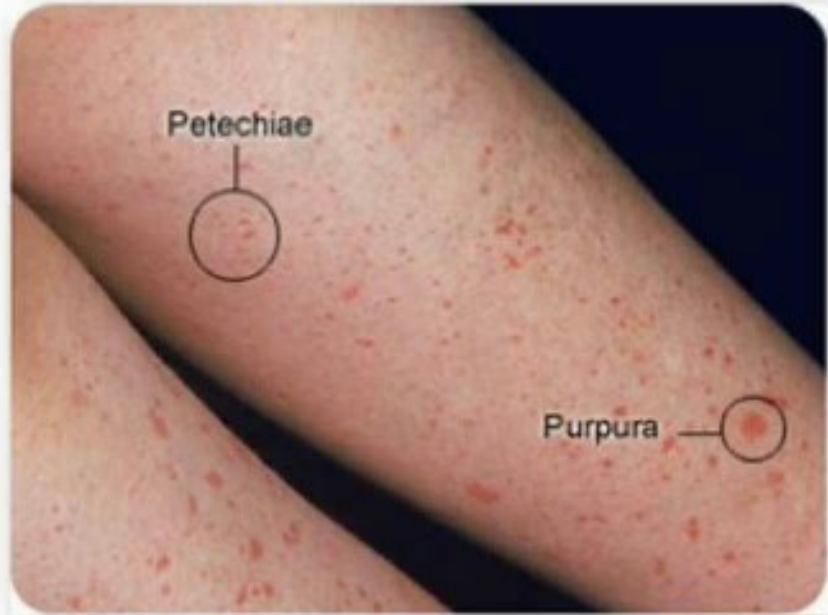
Bleeding



NO

Splénomegaly

Petechiae in dependent areas
where capillary pressure is high



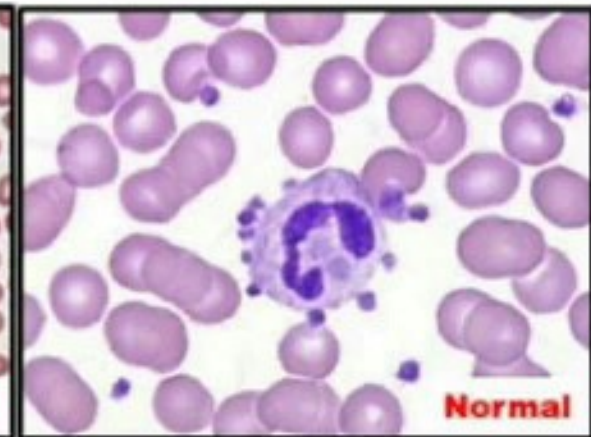
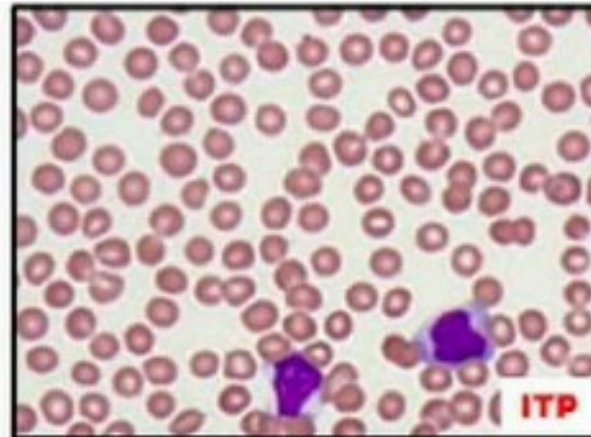
Special Investigations



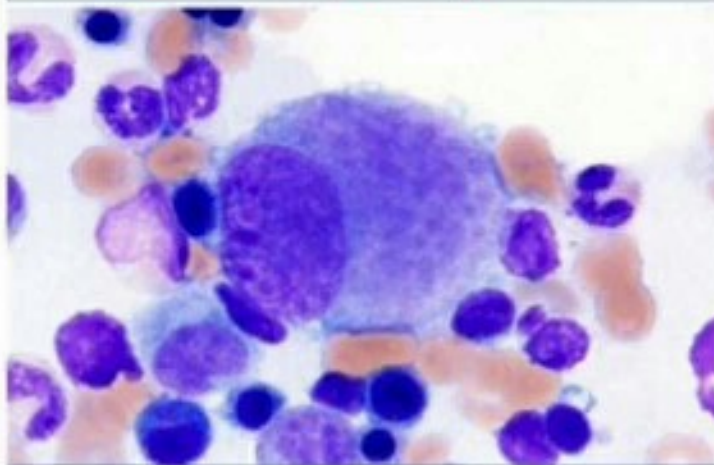
Bleeding Time



Platelet Number



Megakaryocytes



Bone marrow

Treatment

- 1 **Corticosteroids**
 - 2 **Splenectomy**
 - 3 **High dose IV Immunoglobulins**
- In emergency situations
e.g. preparation for surgery**
- 4 **Danazol may be effective in some cases**



Bleeding Tendency

Henoch- Schonlein purpura (HSP)



Dr. Tarek Abdelhamid M.D.

Definition

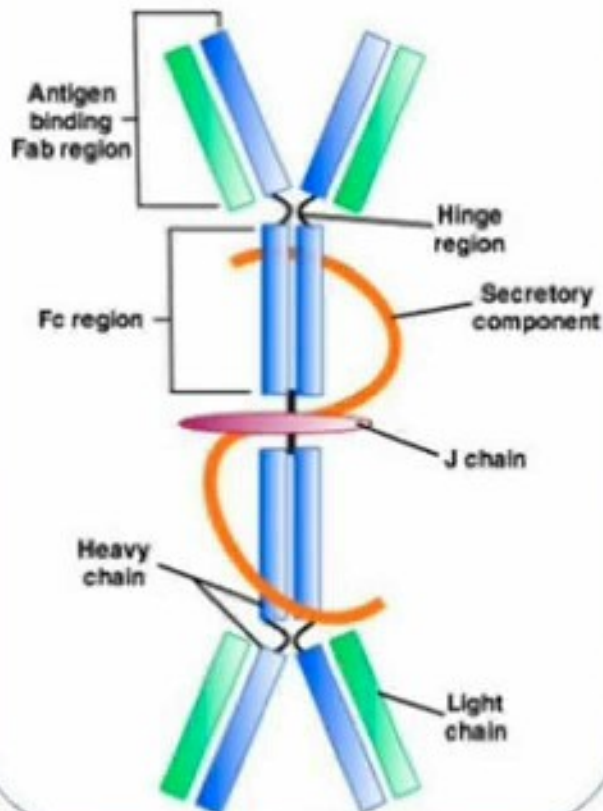
Allergic form of purpura associated with allergic manifestations e.g.

- ① Allergy
- ② ADGN
- ③ Acute abdominal pain
- ④ Arthritis

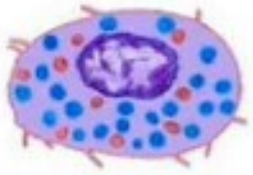
Aetiology

The condition may occur in response to **a recent RTI or GIT** infection that increases the production of IgA (Typically in children)

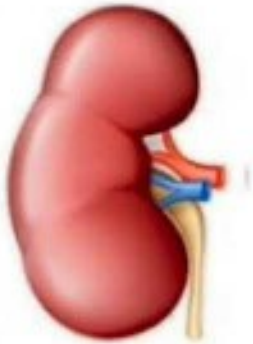
IgA



Clinical Picture



Allergy



ADGN



**Acute
abdominal
pain**



Arthritis

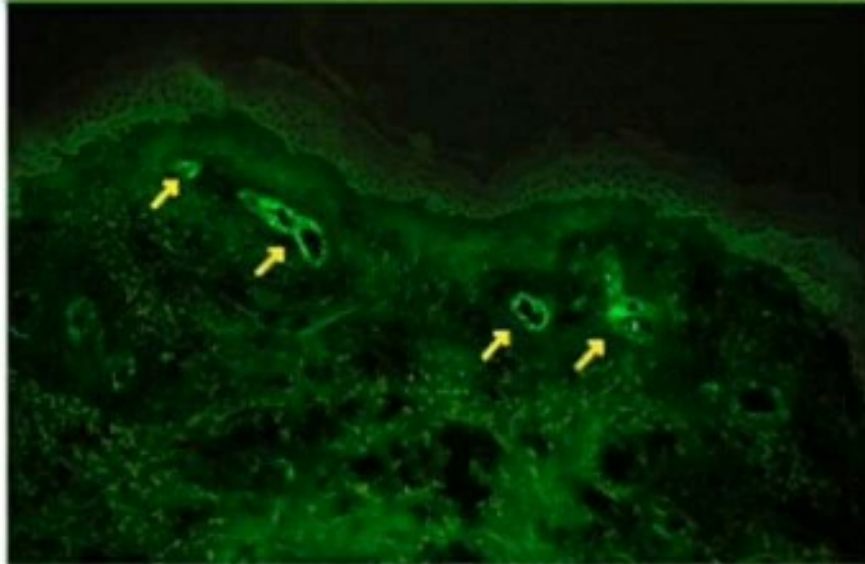


Special Investigations



**Bleeding
Time**

Skin Biopsy



Treatment

The problem is usually self limited, however, corticosteroids may be useful in severe cases



Bleeding Tendency

Hemophilia A



Definition

An X-Linked Recessive disorder characterized by Deficiency of factor VIII (Factor VIII:C or coagulant protein) causing widespread bleeding tendency.

XR

Mechanism

**Defect
in DNA**



 **Factor VIII
Synthesis**

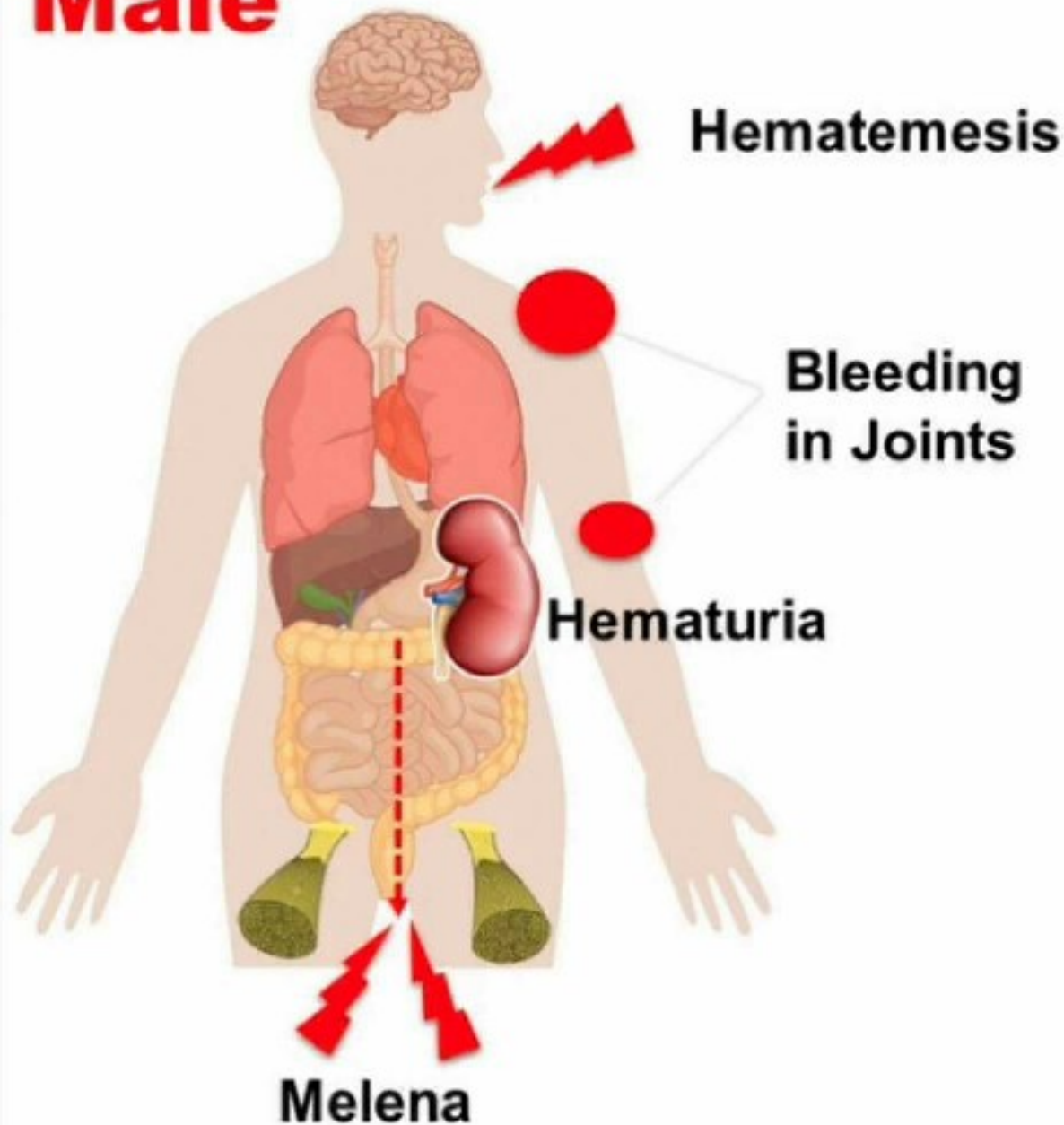


Bleeding everywhere

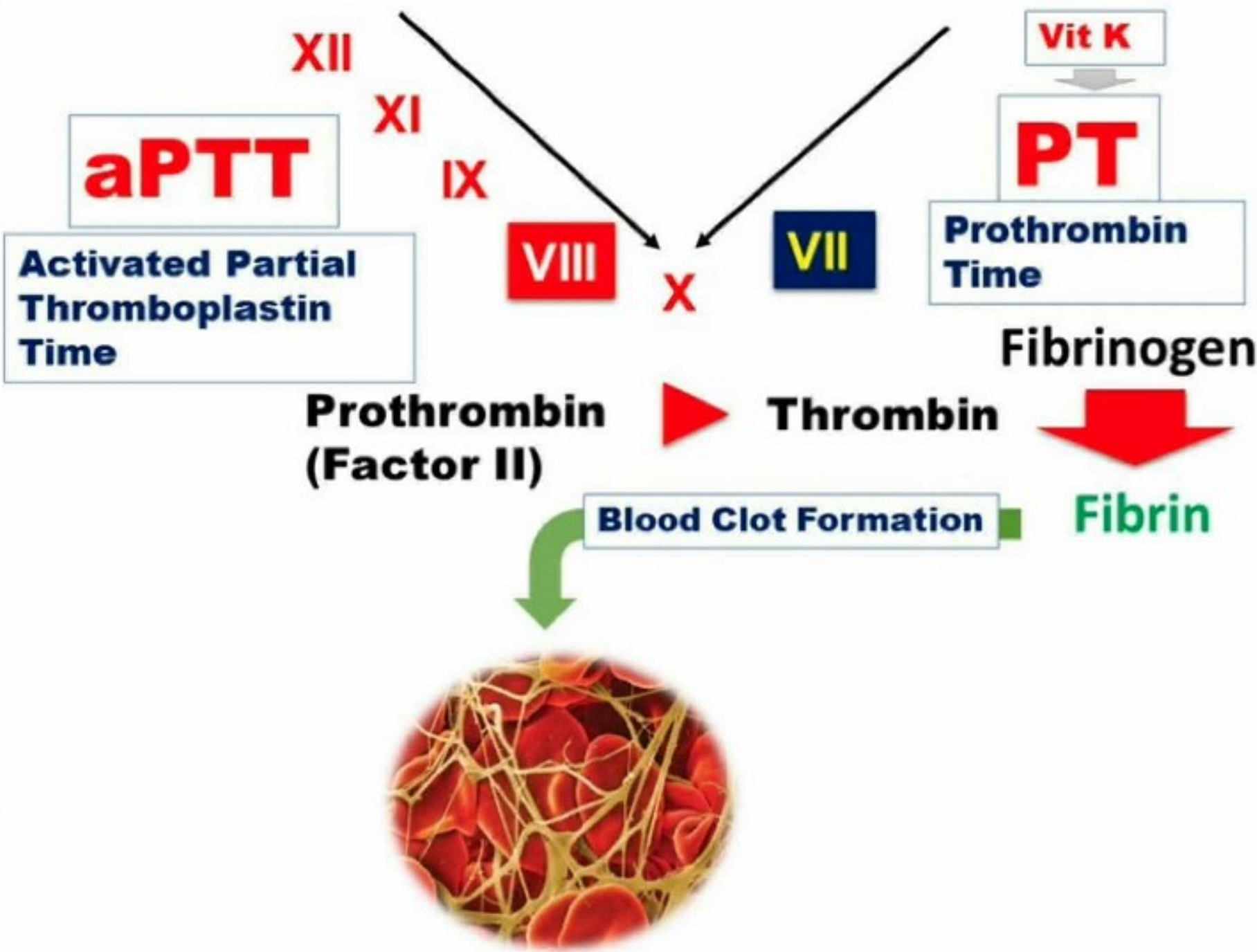


Clinical Picture

Male



**Spontaneous
bleeding any
where especially
in Joints-
Muscles- GIT**



Special Investigations



PTT



**Bleeding
Time**



**Platelet
Count**



**Factor
VIII**

Treatment

Replacement therapy for Factor VIII (for mild cases you can give DDAVP as it releases Factor VIII).

Note

Failure to correct the  PTT after mixing the patient's blood with normal plasma should make you suspect the presence of **Factor VIII Inhibitors** (e.g. in **SLE**)

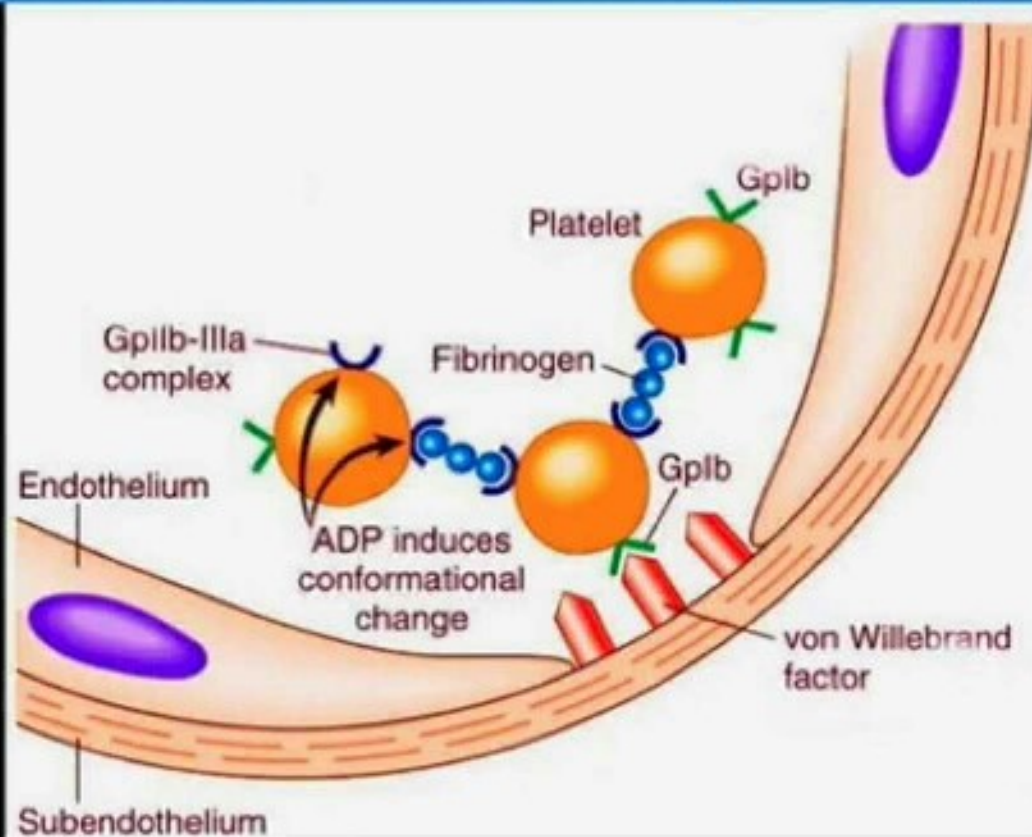


**Add
Normal
Plasma**

Blood

Bleeding Tendency

Von Willebrand disease (VWD)

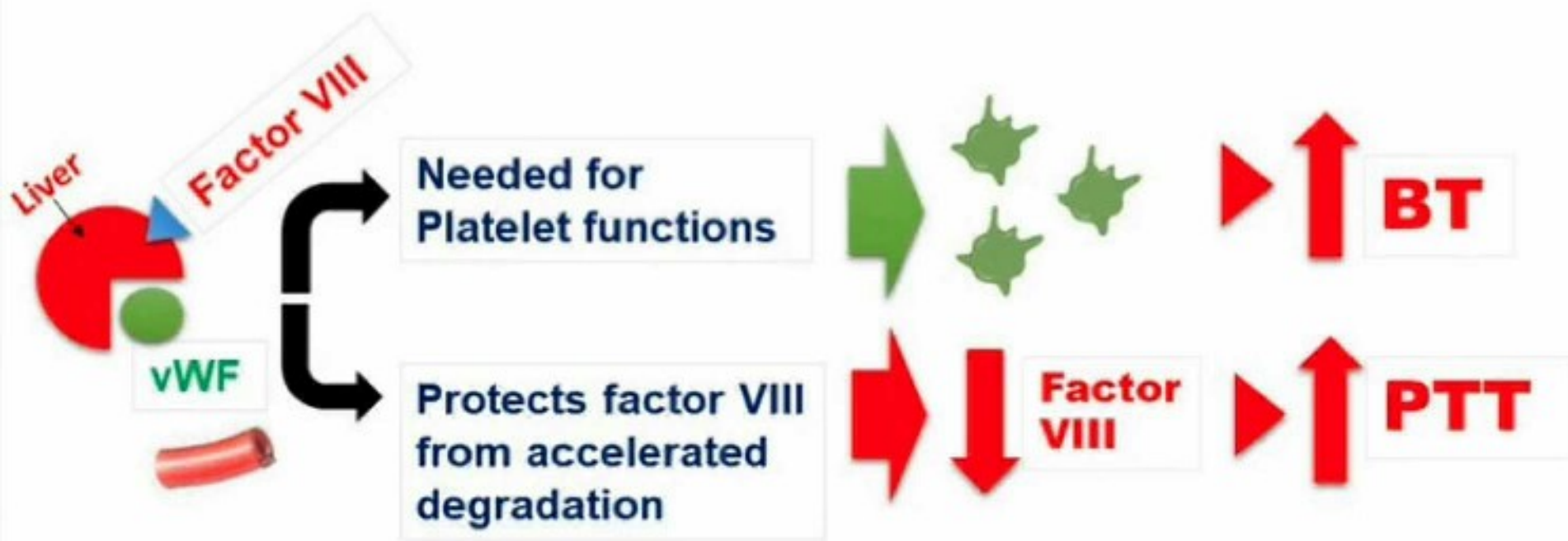


Definition

A mild bleeding disorder caused by deficiency of vWF and is typically associated with mucosal type of bleeding.

AD

Mechanism



Clinical Picture

Epistaxis



Gingival
Bleeding



Purpura



Menorrhagia



**+ve Family History
is Usually present**

Special Investigations



PTT



**Bleeding
Time**



**Platelet
Count**

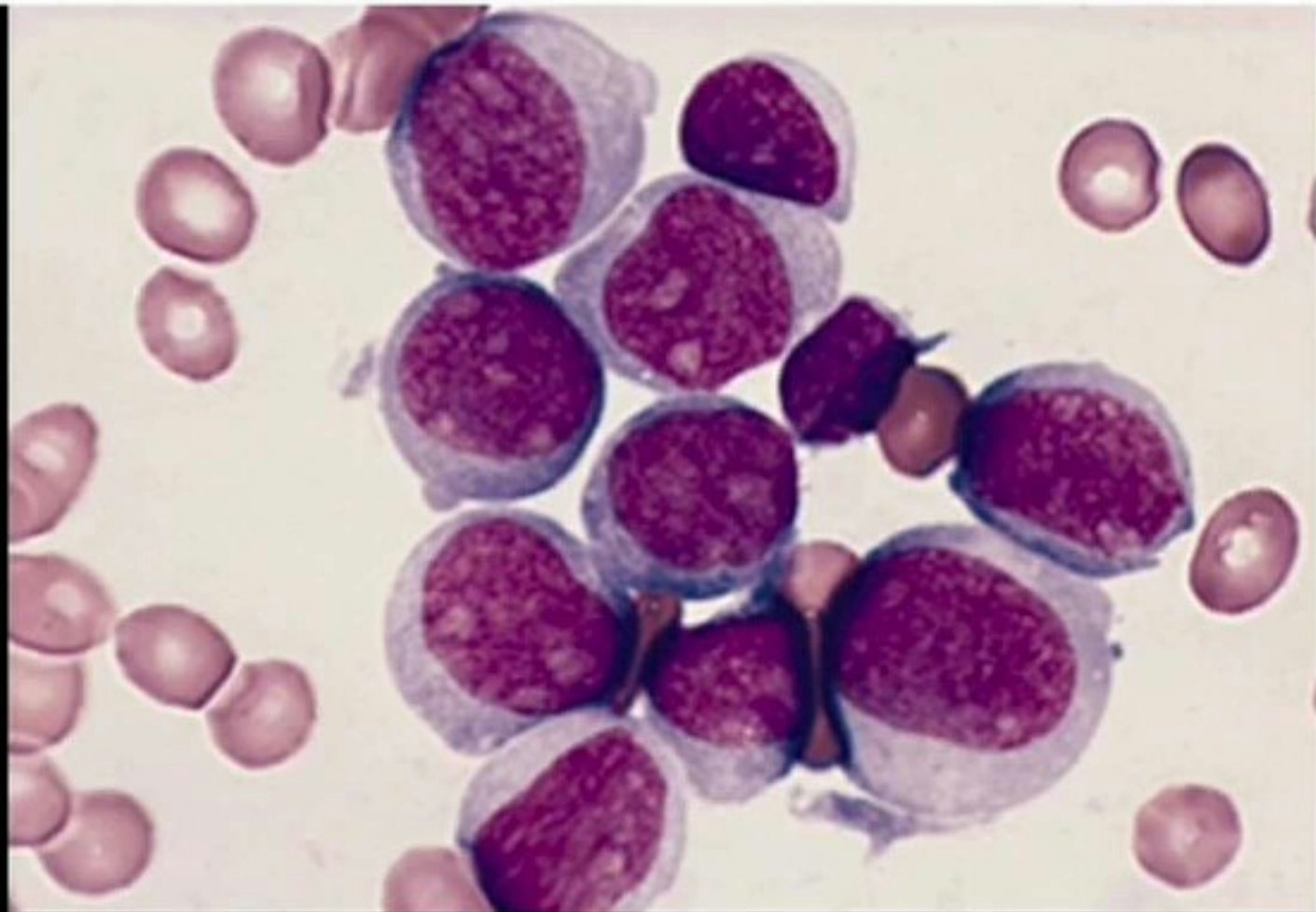


vWF

Treatment

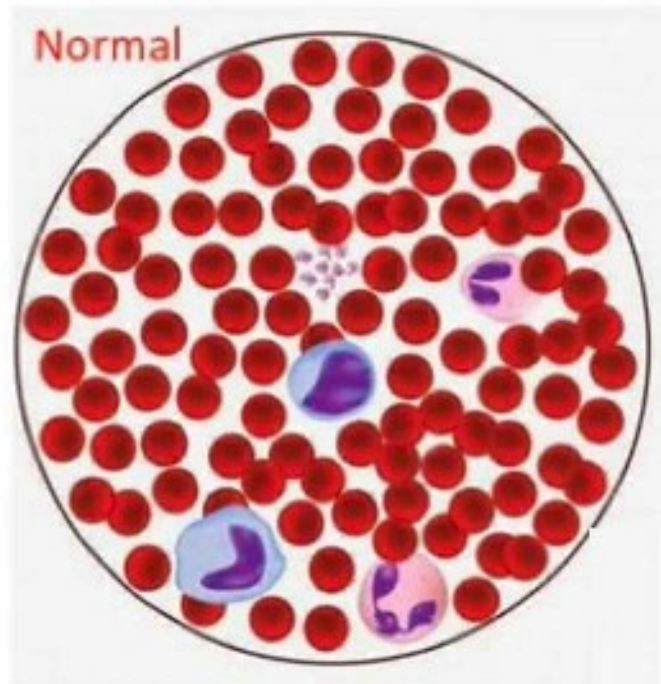
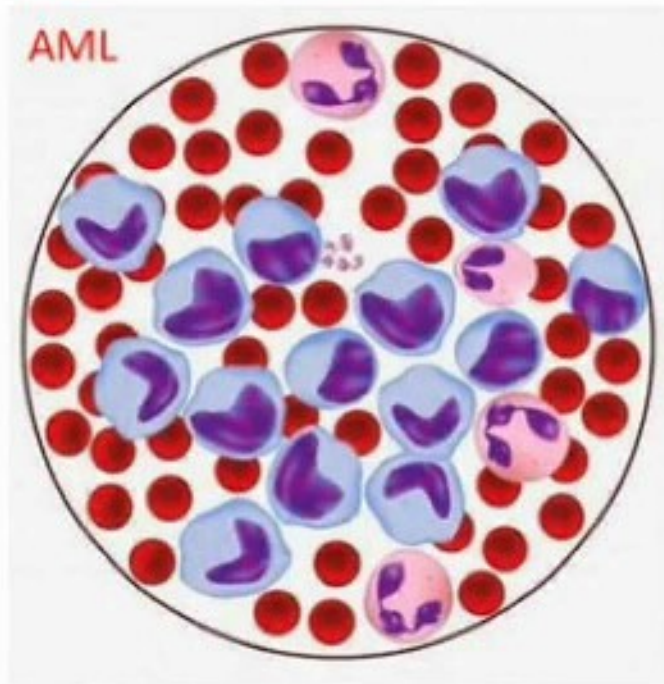
- 1 **No treatment is usually needed**
- 2 **Avoid** Aspirin as it inhibits platelet functions
- 3 **Desmopressin Acetate** to increase the release of vWF from endothelial cells (can be used before surgery to avoid excessive bleeding)
- 4 **Factor VIII concentrates** could be used in severe conditions
- 5 **Antifibrinolytic agents** (Tranexamic acid) may be an adjunct treatment.

Acute Myeloid Leukemia



Definition

Leukemias are characterized by neoplastic proliferation of abnormal WBCs. AML represents a malignancy of hematopoietic progenitor cell in Bone Marrow.



AML occurs mostly in adults (accounts for 80% of adult acute leukemias)

Aetiology

- 1 Most commonly “Idiopathic”
- 2 Benzene
- 3 Irradiation

Mechanism

Local
Compression of
surrounding
bone marrow



PCP



RBCs: Anemia



WBCs Infections



Aleukemic leukemia



Platelets: Bleeding
tendency

Mechanism

Lysis of huge
number of cells
(Release of
endogenous
pyrogens)



Fever

Mechanism

**Infiltration of
Distant Organs
by leukemic cells**



- ① Hypertrophied
bleeding gums**
- ② GLA**
- ③ Splenomegaly**
- ④ Hepatomegaly**
- ⑤ Meningeal
irritation**

Mechanism

**Very high
number of
leukocytes**



**Slow
circulation**



**Headache &
Confusion**

Mechanism

Bone Infiltration



**Bone and sternal
tenderness**

Clinical Picture

Fever

Headache &
Confusion

Meningitis-Like
Symptoms

Exophthalmos

Hypertrophied
bleeding gums

Sternal
Tenderness

Pericardial effusion

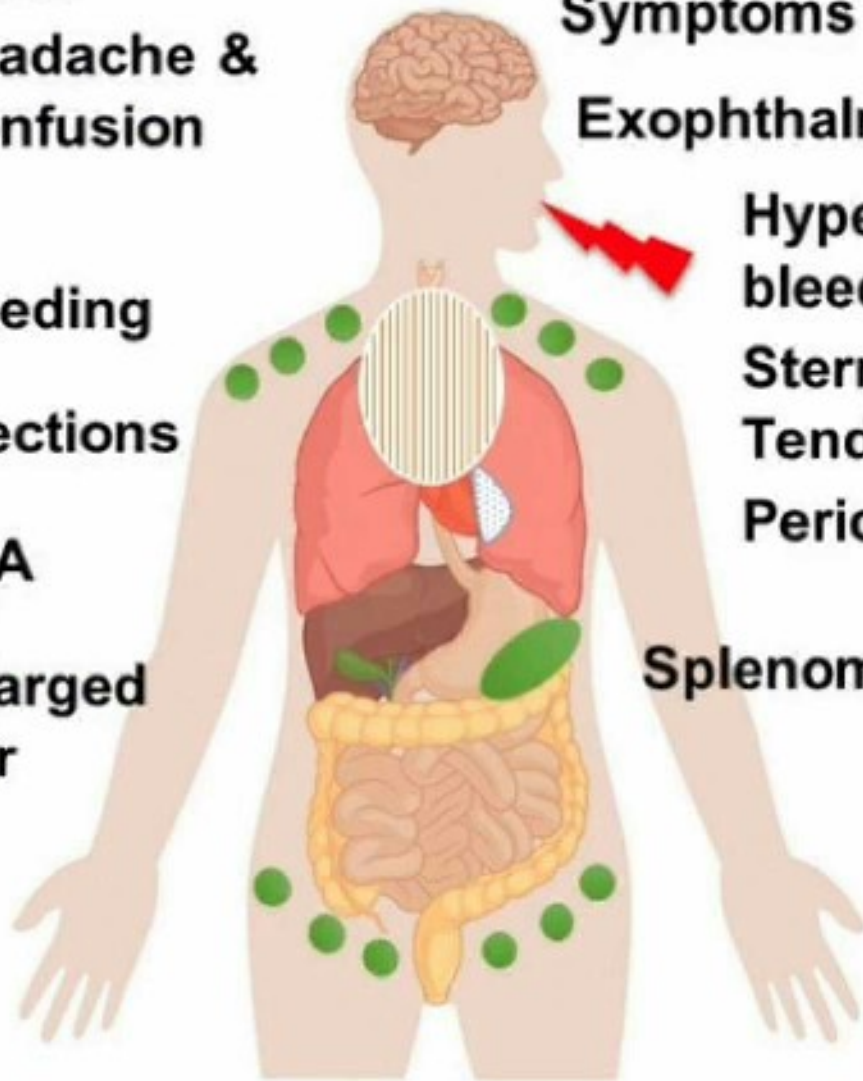
Bleeding

Infections

GLA

Enlarged
liver

Splenomegaly



Special Investigations

PCP

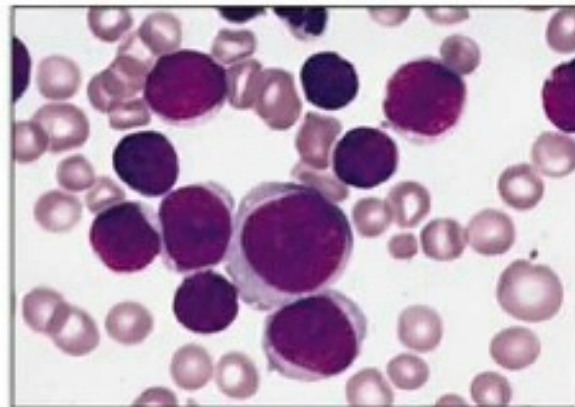


**Leukocytosis
20000-100000**

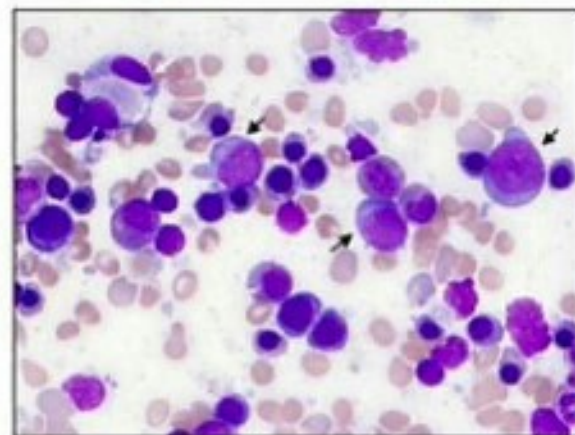
**Blast Cells in
Peripheral Blood
(More than 90%)**

**More than 20% or
more leukemic
blasts in the bone
marrow**

**+ve
Myeloperoxidase
Test**



**Peripheral
blood**



**Bone
Marrow**

Treatment

Note: Very high dose of **Retinoic Acid** (a Vit A analogue) can be used to treat Acute Promyelocytic leukemia.

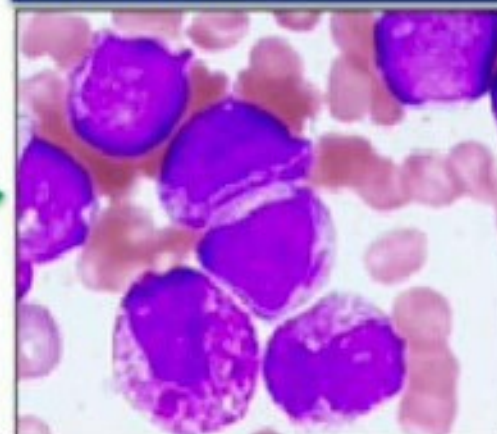
Chromosomal
Translocation
t (15,17)



Abnormal
Retinoic
Acid
Receptors

Block cellular
differentiation
in the bone
marrow

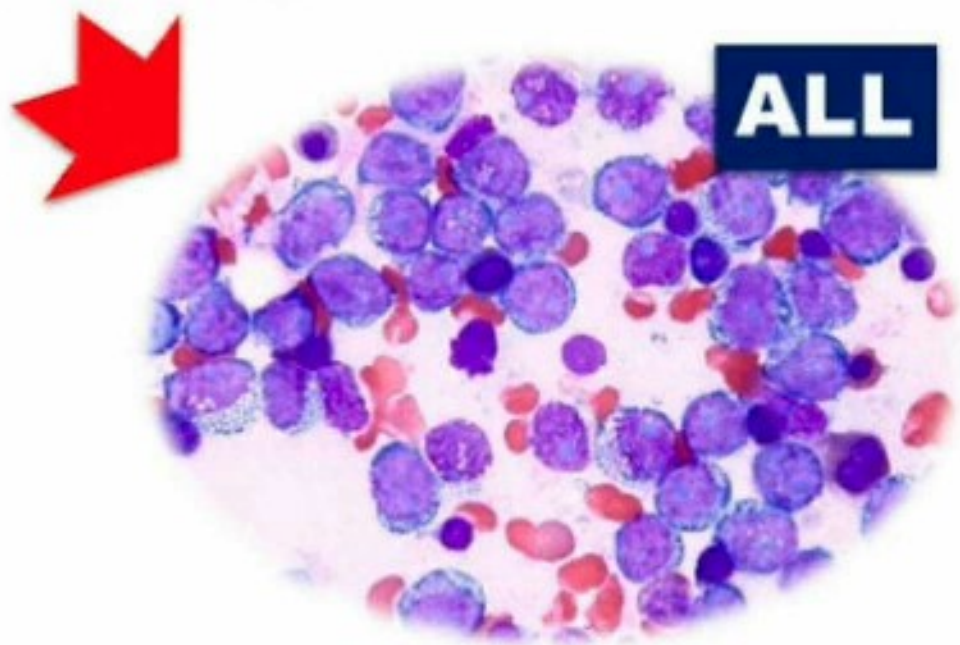
**Acute
Promyelocytic
leukemia**



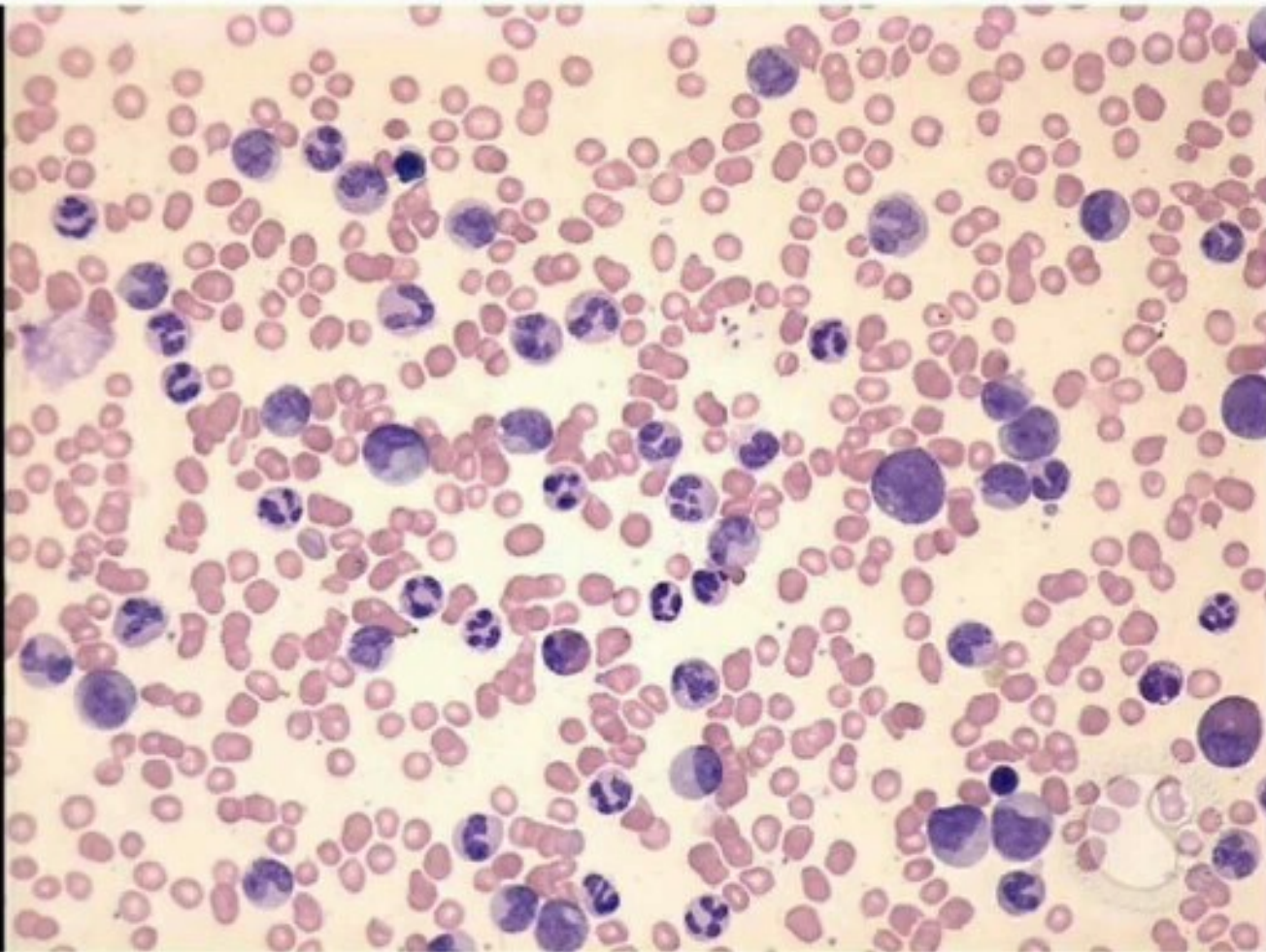
Fusion gene
PML-PAR

ALL

- ① ALL is a neoplasm of early lymphocytic precursors.
- ② Predominance of **Lymphoblasts**
- ③ ALL is the most common malignancy in **children** under age 15 in the United States
- ④ It is the leukemia **Most responsive to therapy**



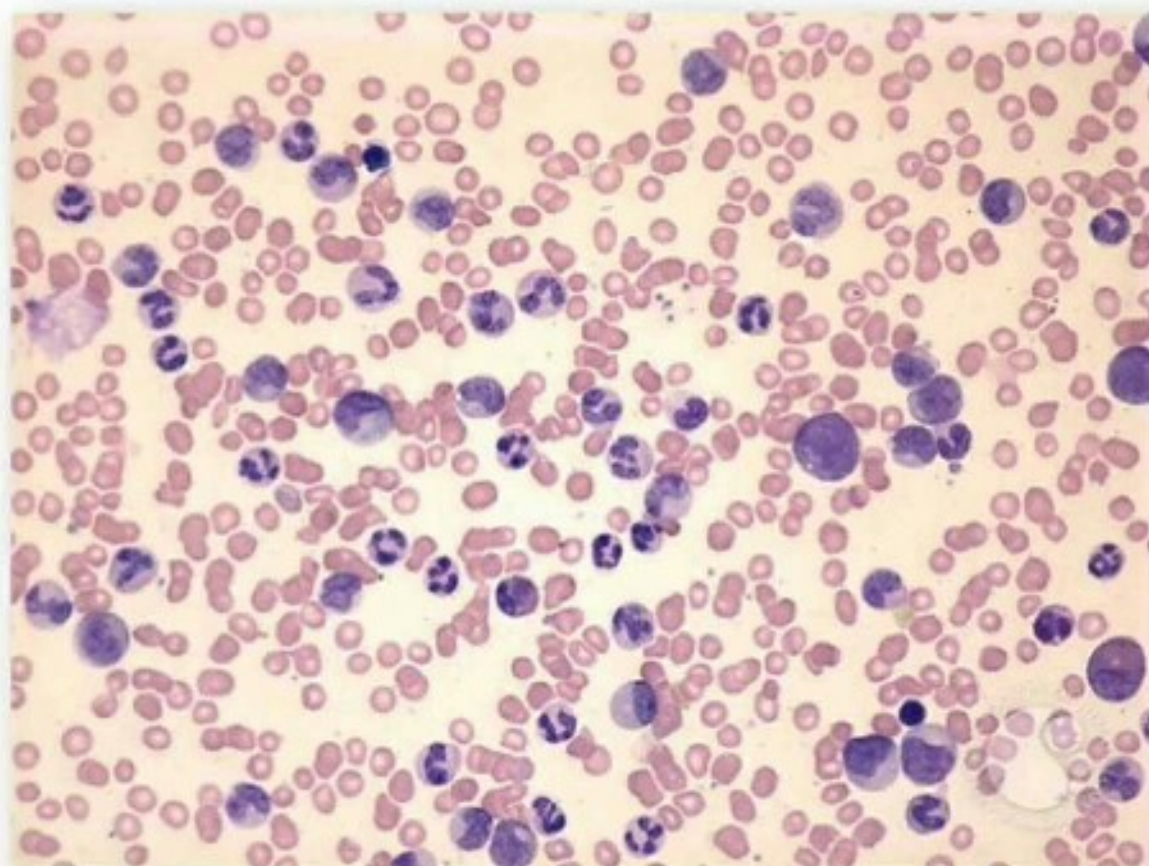
Chronic Myeloid Leukemia



Dr. Tarek Abdelhamid M.D.

Definition

A myeloproliferative disorder characterized by overproduction of myeloid cells

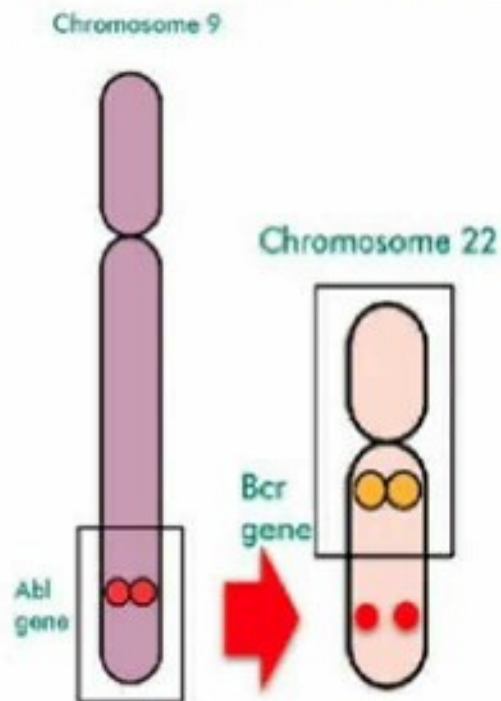


Chronic Myeloid Leukemia

Aetiology

Unknown but many cases are related to the presence of Philadelphia Chromosome (t 9:22)

Philadelphia Chromosome



Philadelphia Chromosome



**Bcr-abl
Proto-oncogene**

**Tyrosine
Kinase
Activity**

CML

Mechanism

**Huge number of
cells increases
the body BMR**



**Low grade fever
Fatigue
Night sweats**

Mechanism

**Infiltration of the
Spleen**



**Marked
Splenomegaly**

Mechanism

If Very high number
of leukocytes (More
than half million/ μ l



leukocytosis



Slow
circulation



Headache
Confusion
Blurring of vision
Respiratory distress

Mechanism

**Obstruction of
corpora
cavernosa by
clubs of WBCs**



Priapism

Mechanism

Increase production
of Transcobalamine II
by the granulocytes



Mechanism

**Increased protein
turnover
(secondary to
increased WBCs)**



Uric acid



Gout

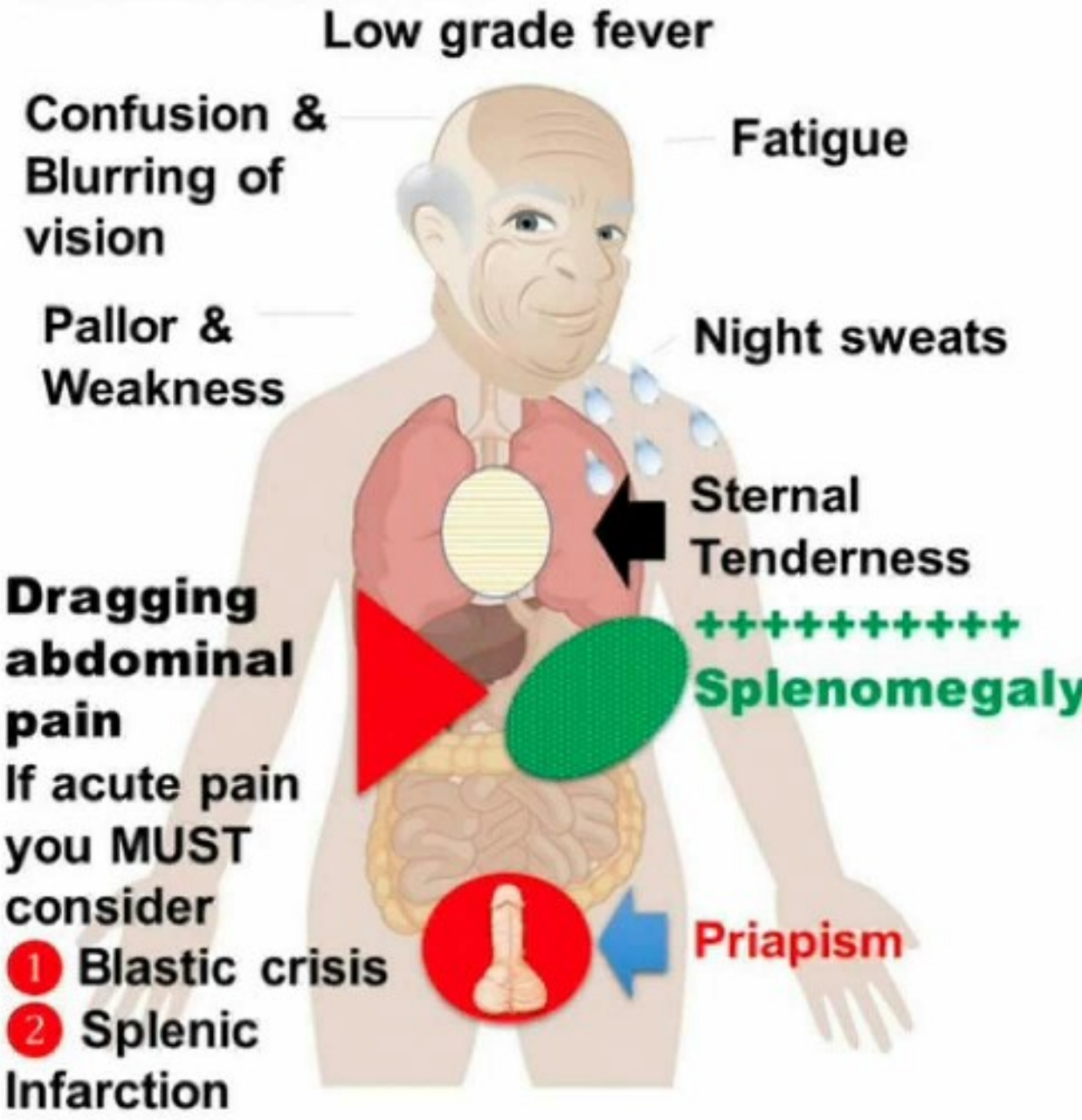
Mechanism

**Expansion of
Bone Marrow**



**Sternal
tenderness**

Clinical Picture



Special Investigations

Blood picture

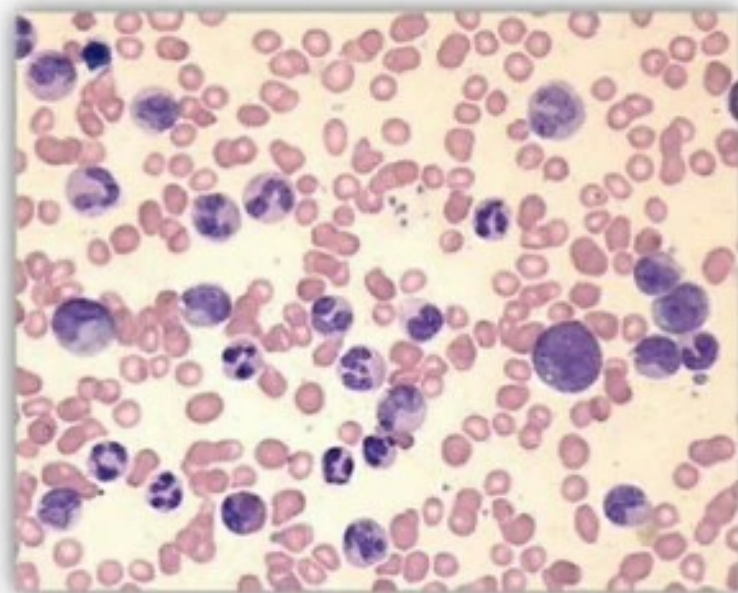
- 1 WBCs 100,000-500,000/ μ l
- 2 **PMNLs 50%**
- 3 Increased Myelocytes 10%
- 4 Blast cells less than 5%
(**except** in Blastic crisis)

**+ve Philadelphia
Chromosome**

 **LAP**

 **Serum Vitamin B12**

Mild anemia (NN) –
+++ESR-
Blood Platelets



Treatment

- 1 Cytotoxic Drugs: Myleran
- 2 Splenic Irradiation
- 3 **Recently**: STI571 (**Imatinib Mesylate**) has been reported to decrease Tyrosine Kinase activity and thus results in dramatic improvement in patients with CML.

Polycythemia Rubra Vera



Dr. Tarek Abdelhamid M.D.

Definition

A myeloproliferative disorder characterized by increase in **ALL** blood elements especially RBCs.

Mechanism



**Blood
Volume**



**Engorged neck veins
Plethoric face
Headache
Hypertension ...Heart Failure
Engorged organs:
Hepatosplenomegaly**

Mechanism



**Destruction
of cells**



**Increased Uric Acid...Arthritis
Increased Vit B12 and
Transcobalamine (due to
release from granulocytes)**

Mechanism



Basophils

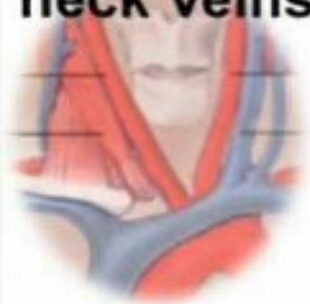


Release of Histamine

- ① Severe itching: especially after hot bathes
- ② Peptic ulcer

Clinical Picture

Congested
neck veins



Slow thinking
& Vertigo
headache

Plethoric face

Venous thrombosis

Coronary- Cerebral- Mesenteric- Pulmonary

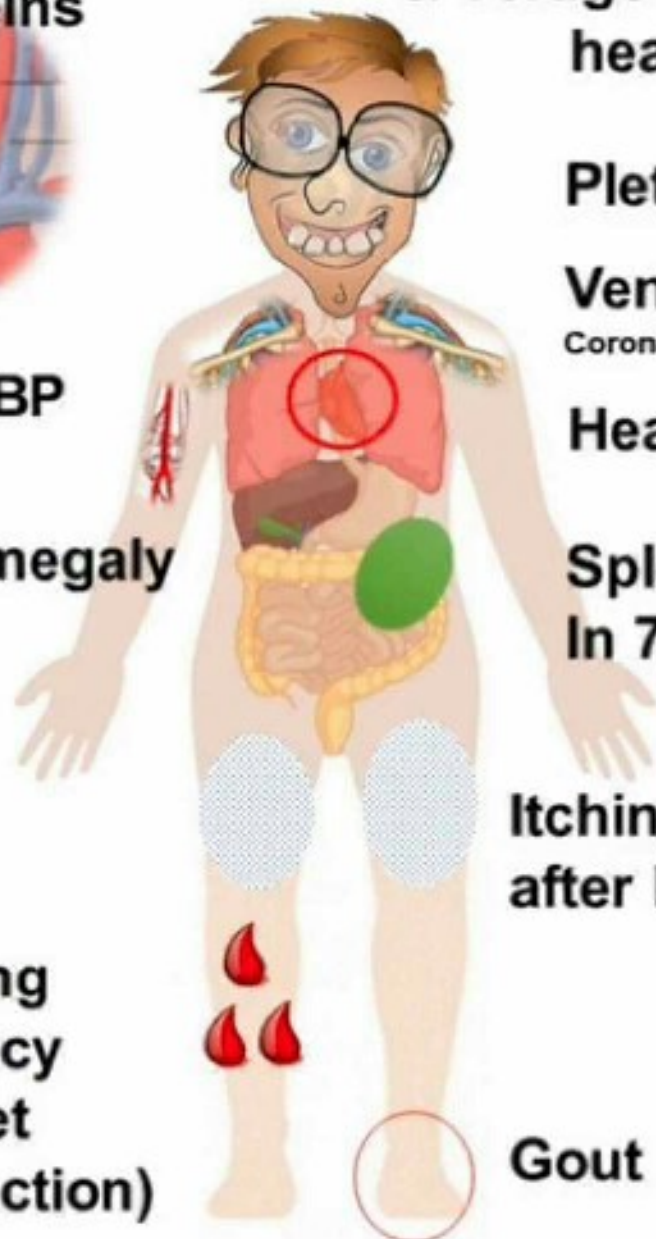
Heart Failure

Splenomegaly
In 75% of cases

Itching especially
after hot bathes

Bleeding
tendency
(Platelet
dysfunction)

Gout



BP

Special Investigations



RBCs-WBCs- Platelets

Hematocrit & red cell mass



Arterial O2 Saturation

Unlike secondary polycythemia caused by Chronic Hypoxemia (e.g. COPD)-
Low O2 saturation + ONLY RBCs are elevated



Erythropoietin level

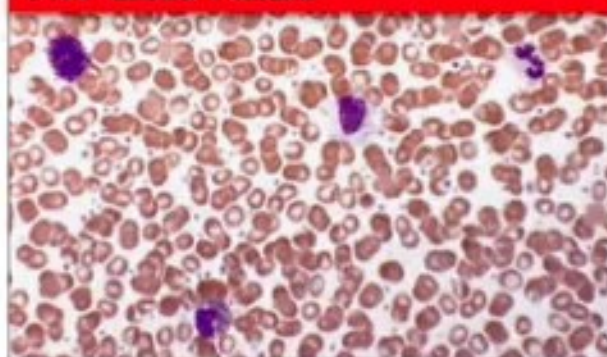


LAP

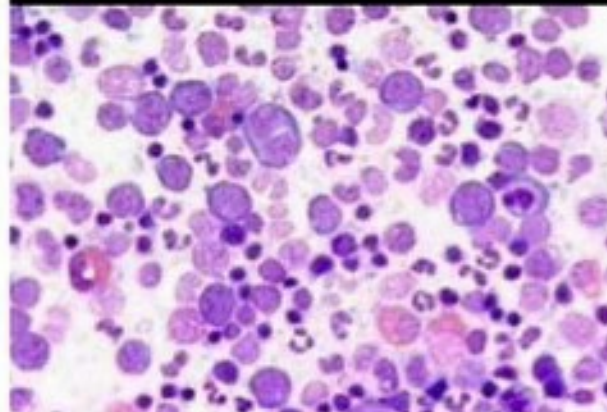
**Unlike
CML**

- 1 **Low** cholesterol level
- 2 Increased Vitamin B12 & Transcobalamine
- 3 Increased Uric Acid level

PRV- Blood Picture



PRV- Bone marrow



Note Causes of Secondary Polycythemia



Cigarette smoking

Chronic Hypoxemia e.g. COPD & CCHD

Cortisone ↑ ↑ ↑

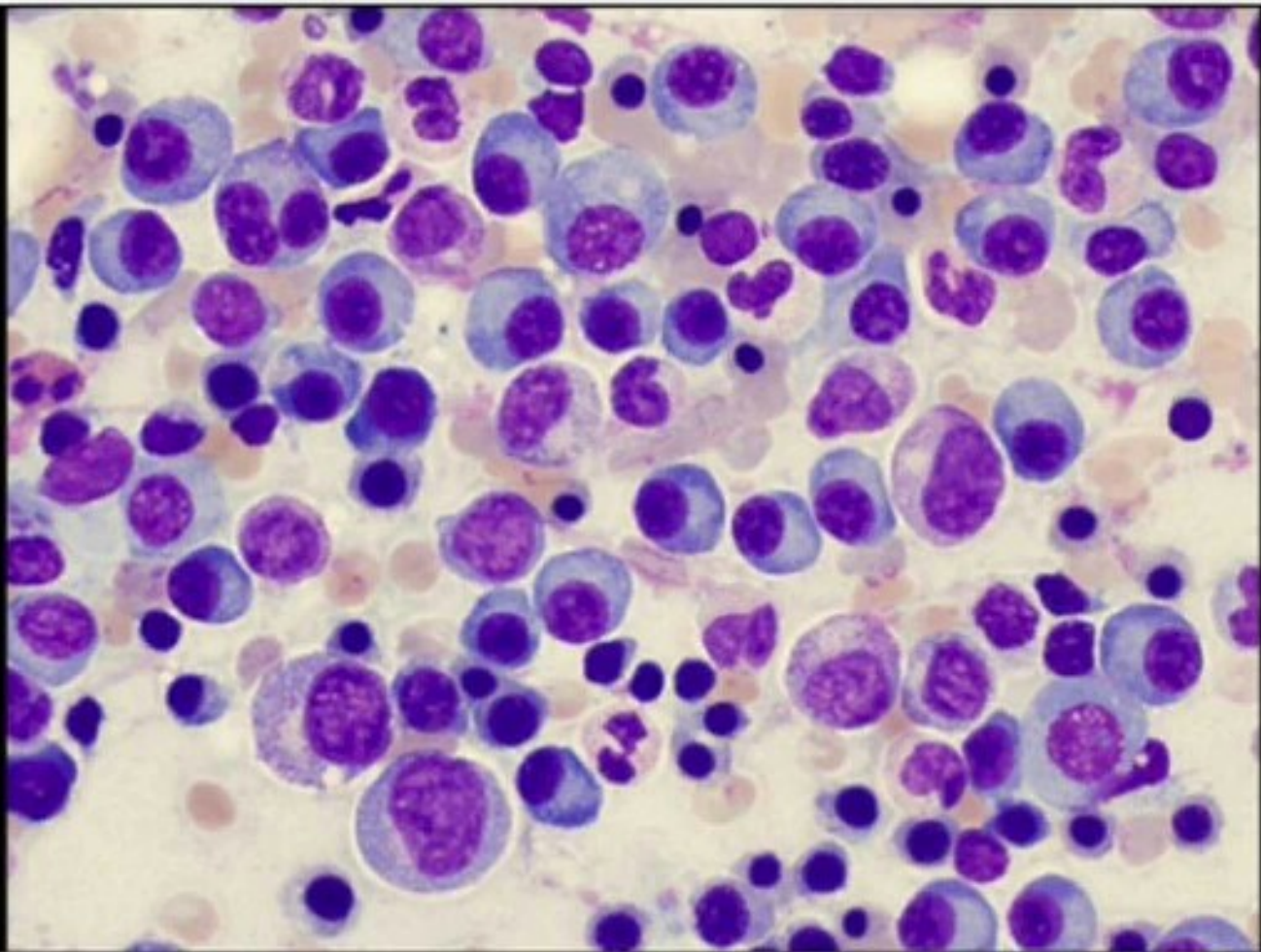
Cancers secreting Erythropoietin

Treatment

- Repeated **venesection** to decrease the number of RBCs
- **Hydroxyurea** to suppress the hyperactive bone marrow
- Low dose aspirin (for thrombosis)
- Allopurinol to decrease elevated uric acid level
- Antihistaminics to diminish pruritus

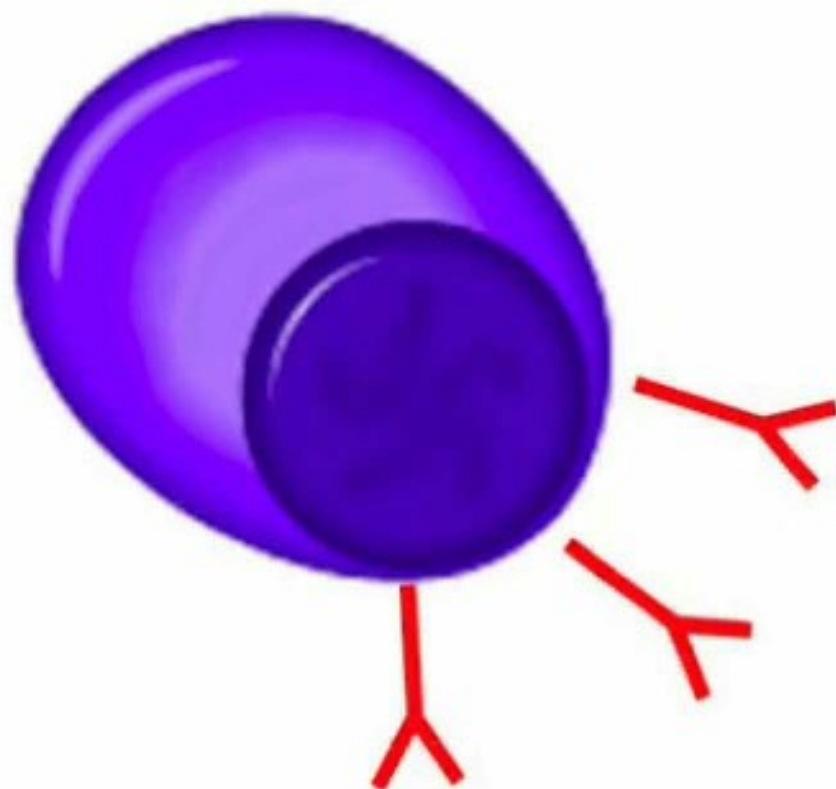


Multiple Myeloma



Definition

A hematological disorder characterized by malignant proliferation of plasma cells which may cause overproduction of immunoglobulins especially IgG (Paraproteins) Light Chains, Uric acid, and OAF.



Mechanism

**Compression
of surrounding
bone marrow**



PCP



RBCs: Anemia



WBCs: Infections



**Platelets:
Bleeding tendency**



Mechanism

**Bone damage
Secondary to
increased OAF**



**Pathological fractures
Osteolytic skull lesions
Hypercalcemia**

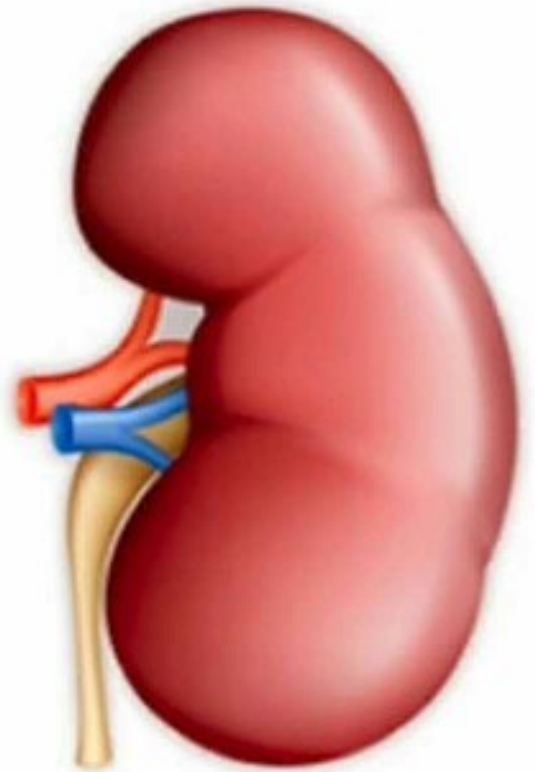
Mechanism

Renal damage



Due to:

- ① Ca deposition in renal tissues
- ② Toxic effect of Light Chains on Renal tubules
- ③ Uric acid nephropathy



Mechanism

**Light
Chains**



**Light chains may pass in
urine causing the
appearance of BJP**

Mechanism

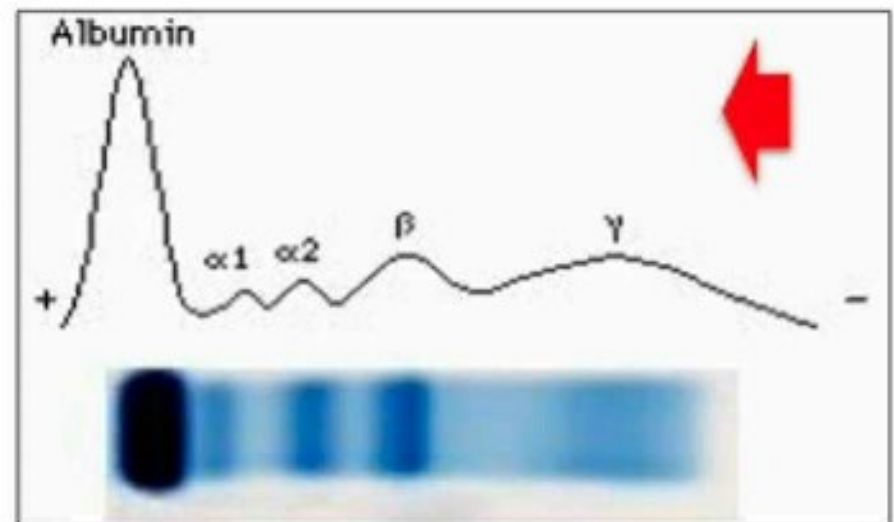
**Light
Chains**



**Light chains may pass in
urine causing the
appearance of BJP**

Mechanism

Production of single form of Immunoglobulins



- 1 A spike on paper electrophoresis (**M Band**) or Monoclonal band
- 2 Suppression of production of other forms of immunoglobulins causing **Infections**
- 3 **Increased blood viscosity**
(especially if it produces **IgM**-IgM Paraproteinemia)
causing confusion-
visual disturbance-
and Vertigo.

Treatment

**CYTOTOXIC
DRUGS**